[JP,11-505610,A]

CLAIMS

[Claim(s)]

1. They are a continuous substrate and a sensor platform which includes a plane and an inorganic dielectric waveguide by permeability, a) An inorganic dielectric waveguide is divided into at least two waveguide fields in a measurement region at least by said permeability, It is divided by fact that an effective refractive index of a field where a wave is guided is larger than the surrounding field, or division of said waveguide is performed by substance on the surface which absorbs incident light.;
b) Said waveguide field is provided with one incidence grating or a common incidence grating, respectively so that it may be maintained after a propagating direction of a wave vector entering.;
c) A sensor platform which is characterized by providing said waveguide field with one outgoing radiation grating or a common outgoing radiation grating, respectively in a suitable case.

2. Sensor platform according to claim 1 being arranged by shape of strip, rectangle, circle, ellipse, or chessboard pattern where said waveguide field became independent.

3. Sensor platform according to claim 2, wherein said waveguide field is arranged by shape of parallel strip.

4. Sensor platform according to claim 1, wherein said waveguide field is arranged by shape of parallel strip joined at end or both ends.

5. Sensor platform according to claim 1 which division into two or more waveguide fields is realized by change of effective refractive index between said waveguide field and its adjoining material, and is characterized by difference of said effective refractive index being larger than 0.2 unit.

6. Sensor platform according to claim 1, wherein division into two or more waveguide fields is realized with absorbent material on the waveguide surface.

7. Sensor platform according to claim 6, wherein division into two or more waveguide fields is realized with metal adhering to colloid on the waveguide surface.

8. Sensor platform according to claim 7, wherein division into two or more waveguide fields is realized with gold adhering to colloid on the waveguide surface.

9. Sensor platform according to claim 7, wherein division into two or more waveguide fields is realized by metal adhering to colloid on the waveguide surface and said surface is embellished by layer of adhesion promoter.

10. The sensor platform according to claim 1, wherein strip width of said waveguide field is 5 micrometers thru/or 5 millimeters.

11. The sensor platform according to claim 10, wherein strip width of said waveguide field is 50 micrometers thru/or 1 millimeter.

12. The sensor platform according to claim 1, wherein the length of each waveguide field of said, which has strip shape, is 0.5 thru/or 50 mm.

13. The sensor platform according to claim 1, wherein the number of strips on said sensor platform is 2 thru/or 1000.

14. The sensor platform according to claim 1 arranging so that said each waveguide field on said substrate may form a multiplex detection area.

15. The sensor platform according to claim 14, wherein each multiplex detection area includes a waveguide field where 2 thru/or 50 became independent.

16. The sensor platform according to claim 14 which has a multiplex detection area of 2 thru/or 100 on said sensor platform.

17. It is the sensor platform according to claim 14 which has the shape of a freely pivotable disk for a central notch (6) as a center, So that two or more multiplex detection can be carried out continuously, if said notch (6) is rotated for said disk as a center in a lower part of an optical apparatus for excitation and detection, A sensor platform to which two or more multiplex detection areas (4) are characterized by a tangential direction or being arranged radiately on said sensor platform.

18. It is the sensor platform according to claim 14 which has the shape of a rectangle or a strip, A sensor platform, wherein a multiplex detection area (4) is arranged on said rectangle or a strip so that two or more multiplex detection can be carried out continuously, if said sensor platform is moved to a transverse direction in a lower part of an optical apparatus for excitation and detection.

19. The sensor platform according to claim 1, wherein said substrate is glass, quartz, or a penetrable thermoplastic plastic material.

20. The sensor platform according to claim 19, wherein said substrate includes polycarbonate, polyimide, or poly methyl methacrylate.
21. The sensor platform according to claim 1, wherein said refractive index is the same about all the waveguide fields.
22. The sensor platform according to claim 1, wherein a refractive index of said waveguide field is larger than two.
23. The sensor platform according to claim 22, wherein said waveguide field includes TiO_2, ZnO, Nb_2O_5, Ta_2O_5, HfO_2, or ZrO_2.
24. The sensor platform according to claim 23, wherein said waveguide field includes TiO_2 or Ta_2O_5.
25. The sensor platform according to claim 1, wherein thickness of said waveguide field is 40 thru/or 300 nm.
26. The sensor platform according to claim 25, wherein thickness of said waveguide field is 40 thru/or 160 nm.
27. The sensor platform according to claim 1, wherein abnormal-conditions depth of said grating is 3 thru/or 60 nm.
28. The sensor platform according to claim 1, wherein a ratio of abnormal-conditions depth to thickness of said waveguide is 0.5 or less.
29. The sensor platform according to claim 1, wherein a ratio of abnormal-conditions depth to thickness of said waveguide is 0.2 or less.
30. The sensor platform according to claim 1, wherein a cycle of said grating is 200 thru/or 1000 nm.
By permeability on the a aforementioned sensor platform, 31. A plane, An inorganic dielectric waveguide field is mutually classified along with a test section by change in at least 0.6 of a refractive index, b). [whether each field is provided with one piece or two independent grating couplers, and] Or it has one piece or two common grating couplers in all the whole field, c) The sensor platform according to claim 1 characterized by a ratio [as opposed to / thickness / in a plane and an inorganic dielectric waveguide field / 3 thru/or 60 nm and thickness in 40 thru/or 160 nm and abnormal-conditions depth of said grating] of abnormal-conditions depth being 0.5 or less by said permeability.
32. The sensor platform according to claim 1, wherein said waveguide field guides one thru/or the three modes.
33. A manufacturing method of the sensor platform according to claim 1 which includes vapor-depositing an inorganic waveguide material in a vacua under

a mask constituted appropriately.

34. In order to form a continuous layer in the first step, an inorganic waveguide material is vapor-deposited, Then, a manufacturing method of the sensor platform according to claim 1 which includes dividing the aforementioned layer into each waveguide field by mechanical scratching, material processing by laser, lithography processing, or plasma etching.

35. A manufacturing method of the sensor platform according to claim 1 which includes making inorganic absorptivity metal adhere on said surface from a colloidal solution with a method constituted appropriately.

36. A manufacturing method of the sensor platform according to claim 1 which includes that a size of particles makes at least 10-nm gold adhere on said surface from a colloidal solution with a method constituted appropriately.

37. A manufacturing method of the sensor platform according to claim 36, wherein a size of said particle is 15 thru/or 35 nm.

38. A sensor platform which changed, wherein one or more specific binding partners are fixed on the surface of the waveguide field according to claim 1 as a chemical or biochemical recognizing element about one or more same or different quality of an analysis target subject.

39. The sensor platform according to claim 38 which changed, wherein said specific binding partner on the surface of each waveguide field is separated mutually physically.

40. The sensor platform according to claim 38 which changed, wherein a specific binding partner is stationed only one sort on the surface of each waveguide field.

41. The sensor platform according to claim 38 which changed, wherein an adhesion promotion layer is arranged between said waveguide field and said fixed specific binding partner.

42. The sensor platform according to claim 38 which a specific binding partner who did the covalent bond to golden colloid is stationed on said waveguide field, and is characterized by colloid of said gold being smaller than 10 nm and which changed.

43. It is the method of producing the sensor platform according to claim 38 which includes passing said specific binding partner who made it dissolve over said independent waveguide field through a multiplex channel flowing-through cell and which changed, a channel of said multiplex channel cell -- a fluid -- a method dissociating in engineering or physically.

44. How to produce the sensor platform according to claim 38 which includes making said specific binding partner who made it dissolve adhere to said independent waveguide field with a stamp and which changed.
45. It is the method of determining one or more luminescence as either claim 1 or claim 38 in parallel using a sensor platform or a sensor platform which changed of a statement, One or more liquid samples are contacted to one or more waveguide fields on said sensor platform, Excitation light is made [entering excitation light in said waveguide field, and] to penetrate in said waveguide field, How to include exciting in EBANESSENTOFIRUDO photogene fixed on photogene in said sample, or said waveguide field by that cause in parallel, and measuring luminescence which this generated using an optoelectronics device.
46. A way wavelength determines the one or more luminescence according to claim 45, wherein 300 thru/or 1100-nm coherent light is used in parallel for luminescence excitation.
47. A way wavelength determines the one or more luminescence according to claim 46, wherein a 450 thru/or 850-nm laser beam is used in parallel for luminescence excitation.
A functionalized luminescence color 48. A rhodamine; fluorescein derivative; coumarin derivative; JISUCHIRI kana phenyl; stilbene derivative; phthalocyanine; naphthalocyanine; tris (2,2'-bipyridyl) ruthenium chloride, A tris (1,10-phenanthroline) ruthenium chloride, a tris (4,7-diphenyl-1,10-phenanthroline) ruthenium chloride, poly pyridyl / ruthenium complex [, such as poly pyridyl / phenazine / ruthenium complex,]; -- platinum / porphyrin complex; -- the one or more luminescence according to claim 45 choosing from a category which consists of europium and terbium complex; and cyanine dye. How to determine in parallel.
49. How to determine the one or more luminescence according to claim 48, wherein fluoresceinisothiocyanate is used as said luminescence color in parallel.
50. A method according to claim 45, wherein luminescence which was excited in dissipation and emitted isotropic is detected.
51. A method according to claim 45, wherein said luminescence which was recombined in said waveguide and which was excited in dissipation is detected at said sensor platform edge via an outgoing radiation grating.
52. A method according to claim 45, wherein both sides of luminescence

emitted isotropic and recombined luminescence are detected independently, however simultaneous mutually.

53. A method according to claim 45, wherein absorption of said emitted excitation light is judged simultaneously.

54. A method according to claim 45, wherein said luminescence is excited by laser light source with same or different various wavelength.

55. A method according to claim 45, wherein said luminescence is excited by diode laser of a single tier.

56. A method according to claim 45, wherein said sample analyzed is an egg yolk, blood, a blood serum, plasma, or urine.

57. A method according to claim 45, wherein said sample analyzed is alcohol by the surface water of aggregate, soil, a vegetable extract, biological process, or a synthetic process.

58. Use of a sensor platform given in either of claims 1 or claims 38 for a fixed quantity of a biological substance in affinity sensing, or a sensor platform which changed.

59. An antibody or an antigen, a receptor or ligand, a chelating agent, or a histidine marker component, An oligonucleotide, a DNA strand or RNA chain, an analog of DNA or RNA, Use of a sensor platform given in either of claims 1 or claims 38 for a fixed quantity of an enzyme, an enzyme substrate, enzyme cofactor or enzyme inhibitor, lectin, and carbohydrate, or a sensor platform which changed.

60. Use of a sensor platform given in either of claims 1 or claims 38 for an alternative fixed quantity of luminescent components [in / optically / an opaque fluid], or a sensor platform which changed.

DETAILED DESCRIPTION

[Detailed Description of the Invention]

A sensor platform and a method for parallel detection of two or more quality of an analysis target subject which used the luminescence excited in dissipation This invention, It is related with the sensor platform on the basis of at least two planes, the independence, and the inorganic dielectric waveguide field on a common substrate, and the method for parallel

dissipation excitation of the luminescence of the same or different quality of an analysis target subject, and detection.

This invention relates to the sensor platform which includes the sensor platform which has again one or more organic phases fixed on a plane, independence, inorganic dielectric waveguide fields, and those fields and which changed. The further object of this invention is use of said sensor platform in the luminescence detecting method for an alternative fixed quantity of quantitive affinity sensing and luminescent components [in / optically / an opaque solution], or said sensor platform which changed.

If a light wave enters in the planate waveguide surrounded by the medium with a low refractive index, the light wave will receive restriction by the total internal reflection in the boundary of a waveguide. The planate waveguide is constituted from the simplest example by the system, a substrate, a waveguide, and the upper layer (or sample which should be investigated), of three layers, and the refractive index of this waveguide is the highest. By an additional interlayer, an operation of this planate waveguide is further improvable.

In this composition, a part of electromagnetic energy enters in a medium with a low refractive index. This portion is called the EBANESSENTO (attenuation) field. The strength of EBANESSENTOFIRUDO is very greatly dependent on the ratio of the thickness of the waveguide itself, and the refractive index of a waveguide and the medium surrounding it. In the case of a thin waveguide (i.e., layer thickness), it is the same as the wavelength guided, or when smaller than it, it can discriminate from the discrete mode of waveguide light.

If EBANESSENTOFIRUDO is used, it is able for a refractive index to excite the luminescence in a low medium relatively, and to excite the luminescence only at the latest of a waveguide field, for example. This principle is known as EBANESSENTORUMINE sense excitation.

Since excitation is limited to the waveguide latest, EBANESSENTORUMINE sense excitation is attracting the big interest in the analytic field. The method and device which determine the luminescence excited like dissipation of the antibody or antigen by which the sign was carried out with the luminescence color are a known thing.

For example, it is described by US-A-4 582 809.

Then, the optical fiber is used for the device by which the application

for patent was carried out for EBANESSENTORUMINE sense excitation. A diameter is usually to 1 millimeter, and such an optical fiber will guide many modes, if a laser beam enters. The luminescence excited in dissipation can be easily measured only by the portion which carried out re incidence into those fibers. I hear that the device is relatively large and comparatively a lot of samples are needed, and there is a still more disadvantageous point. There is almost no room to reduce the size of this device still more nearly substantially, and it is still more so about the miniaturization for integral-type photosensor manufacture.

Increase of sensitivity is generally connected with increase of the size of a device.

A planate optical waveguide is used, and the light measurement apparatus for measuring the luminescence of a biosensor in an EBANESSENTO excitation state is known similarly, for example, it is described by WO90/06503. The waveguide used on these specifications is 160 nm thru/or 1000 nm in thickness, and an excitation wave enters, without using a grating coupler.

In order to increase the sensitivity of the luminescence excited in dissipation, various trials are performed for integral-type photosensor production. For example, to 595 - 607 pages of the by OSEN cers and 6th volume (1991) bioelectronics (Biosensors & Bioelectronics). It is produced by a two-step ionic exchange method, and the planate single mode or waveguide in the low mode in which an excitation wave is entered using prism is described. The affinity system used is the protein A by which human immunoglobulin G / fluorescein sign was carried out, an antibody is fixed on a waveguide, and the protein A which should be detected and by which the fluorescein sign was carried out with a phosphate buffer. The measurement region of a waveguide is added by the film of wrap polyvinyl alcohol.

I hear that it becomes only what has the small difference of a refractive index between a waveguide and a board layer, but sensitivity becomes low relatively as a result, and there is a disadvantageous point in this method which should be taken into consideration.

The sensitivity is protein A 20nM by which the fluorescein sign was carried out. Since it is still insufficient for the judgment of ultralow volume, it is necessary to increase sensitivity further. Reappearance and implementation are difficult for incidence of the light using prism, and

the big reason is because incidence efficiency is dependent on the state and size of a contact surface of prism and a waveguide.
US-A-5 081 Another principle is proposed by 012. Thickness is 200 nm thru/or 1000 nm, the planate waveguide includes two gratings, and one of these is provided with the shape of a reflective grating. As a result, the light wave which entered must pass through the sensor area between these gratings twice [at least], and sensitivity will increase by that cause. I hear that the reflected radiation may bring about the increase which is not desirable as for background radiation intensity, and a disadvantageous point has it.
Description is made by WO91/10122 about the thin layer part photosensor which includes the outgoing radiation grating which carried out remoteness to the incidence grating physically. If an inorganic metal oxide with a high refractive index is used as a waveguide, it is suitable for especially absorption measurement. Various examples suitable for incidence and outgoing radiation of a multicolor light source are described. The suitable thickness of a waveguide is more than 200 nm, and the depth of the grating should be made about 100 nm. In these conditions, since only low sensitivity is obtained, it is not suitable for measurement of the luminescence in affinity sensing. In 4583 - 4589 pages of the 31 No. (1990) with an applied OPUTIKUSU (Appl. Optics) of volume [29th], as for this, the overall efficiency of these systems is checked with the data that it is 0.01% in 514 nm, 0.3% at 633 nm.
In another example of the same sensor, two or more planate polymer waveguides usable as a gas mixture object analyzer are added to a substrate. In this case, change of an effective refractive index or change of the thickness of the polymer waveguide which contacts solvent vapor, for example is used. The structure of a waveguide changes with them physically. However, since such change may cause an incident change and increase of dispersion and may reduce sensitivity greatly, it is completely unsuitable for measurement of the luminescence in affinity sensing.
In the making process of a planate waveguide, the smoothness of a substrate, the fixed thickness of a waveguide and homogeneity, and the refractive index of the material used are very important. This is for example, EP-A-0. 533 It is described by 074 and addition of the waveguide of the minerals to a plastic plate is proposed in this specification. When the composition

of a grating coupler presses this composition fit in a plastic, there is an advantage that it can carry out economically in this. However, in one side, the necessary condition about the optical property of a plastic plate will also increase.

There is a considerable advantage in a planate waveguide about industrial production to the waveguide on the basis of fiber OPUTIKUSU. In particular, in the case of a fiber, in order to realize a perfect optical property, generally, it is necessary [it] to grind an amputation stump part. On the other hand, a planate waveguide can be fractured or cut [whether it pierces in a desired size after that by producing in sheet shape, and]. In many cases, it is unnecessary and the more economical mass production of finishing of an end is attained.

The further advantage of the planate waveguide provided with the grating coupler has simple adjustment of a measuring device, and I hear that coating for fixing for example, the quality of an analysis target subject can carry it out simply, and it has it. Therefore, a standard coating technique which can make reproducible fixed thickness can be used. As an example of such a method, there are spraying, spreading with a knife, spin coating, and immersion. A quality control can also be carried out by the simple method using a known very precise method.

For example, there is a suitable method microscopic or like an interferometer, polarization analysis, or angle-of-contact measurement. Even if these methods cannot be used for the curved surface which is looked at by the waveguide based on fiber OPUTIKUSU or it can use them, they are accompanied by difficulty.

With waveguide itself, the problem that the character of incidence of the light wave to a waveguide is also big is brought about. The requirements about the grating for entering light in the waveguide of the taper of an integral-type photosensor, For example, "the chemical biochemical and ENVAIRON mental phi BASEN cers (Chemical, Biochemical and Environmental Fiber Sensors) V." It is shown in Proc. SPIE, the 2068th volume, and 313 - 325 pages (1994).

The abnormal-conditions depth of a grating and the thickness of the waveguide are deterministically described as an important feature.

Although reference to the luminescence from which the system proposed by this publication is detected is not performed, it can be used, for example

as an integral-type photometer.
When using it for luminescence measurement of such a planate waveguide provided with the integral-type grating coupler, those usefulness and the feature indispensable to realization of high sensitivity are suitable incidence efficiency, the most powerful possible EBANESSENTOFIRUDO, and a low extinction ratio of a guided wave. These features are mainly determined by the combination of a waveguide, a substrate, and an interlayer's refractive index, the thickness of a waveguide, and the structure of a grating coupler, abnormal-conditions depth and grating cycles. There is the flatness or granularity of the optical property which needs the surface, and the surface in other factors.
On the sensor platform of the shape of a homogeneous film, I hear that the inconvenience about all the detecting methods of the luminescence excited in dissipation explained as conventional technology can analyze only one sample at a time at once, and there is. In order to measure further on the same sensor platform, the work of troublesome washing and cleaning is needed. Especially this is applied when detecting qualitatively [from the quality of an analysis target subject measured first / different] of an analysis target subject. Generally in the case of immunoassay, this means that the whole fixed layer on a sensor platform must be exchanged, or a new sensor platform must be used.
For this reason, it is necessary to develop the method, i.e., the method of analyzing without additional cleaning work one after another simultaneous, that two or more samples can be analyzed in parallel. Arranging two or more sample cells which make well shape within the sample plate of the waveguide topmost part, for example on the continuous waveguide is proposed by WO95/03538. Under each sample cell, the grating which emits a part of light guided through the waveguide is located. Detection of the quality of an analysis target subject is performed based on change of the degree of emitting angle as a function of the concentration of the quality of an analysis target subject. The method of being based on change of a refractive index generally has sensitivity clearly lower than a luminescence method.
The device and method for carrying out immunoassay using the fluorescence excited in dissipation, for example are proposed by WO94/27137. This device comprises a continuous optical waveguide which has the two parallel planate

surfaces and a side edge part which acts with the lens as an incidence element. Two or more specific binding partners are fixed by at least one surface. In the suitable example, those specific binding partners are arranged on the continuous waveguide so that it may estrange physically mutually. In the example of use, they are arranged in the waveguide surface wrap punctiform.

If based on the indicated example, it must be assumed that the efficiency attained by incidence passing through this side edge part becomes lower than the case of incidence through a grating. the case where a (self-support type waveguide), the strength of EBANESSENTOFIRUDO, therefore excitation efficiency are single mode waveguides with a thin layer relatively by a layer being thick -- a considerable grade -- it becomes low. As a whole, the sensitivity of this device was limited as a result.

The disadvantage that excitation light excites all the molecules by which the fluorescent substance sign was carried out is among those devices arranged at the waveguide which various specific binding partners followed. Therefore, selection of the measuring place by a position is impossible. The fluorescence photon recombined in dissipation contributes to the signal from the point which adjoined, and brings about an error of measurement.

The planate optical component which made the subject the glass which includes a channel-like waveguide in the integrated optics applied to a telecommunications sector is known, Those waveguide channels are produced by exchanging each ion in the surface using a mask (62nd volume of glass theque niche BERIHITE (Glastechnische Berichte) 285 pages (1989)). The layer which shows the slight increase in a refractive index by that cause in the channel doped with ion and which was linked physically is brought about. Generally this increase is less than 5%. Such a component is complicated and production expense also becomes high.

The 1587th volume of SPIE, In 98 - 113 pages of "chemical biochemical and ENVAIRON mental phi BASEN cers (Chemical, Biochemical and Environmental Fiber Sensors) III" (1991), R.E. Kunz (Kunz) is an optical waveguide which branches and joins again after that, and has described the optical waveguide suitable for especially integrated optics apparatus, such as an interferometer. Such a structure is not suitable for measurement of the luminescence excited in dissipation. The reason is for the intensity of the light wave which entered at the 1st turning point to receive a rapidly

big loss in the composition in which two or more turning points get mixed up impossible [dealing with those elements separately]. The difference angle of such branching is small (usually 3 degrees) one, in the case of a small component, the distance between two branches in branching needs to become small, or it is necessary to enlarge the size of a component according to it, and, generally such a thing is not desirable. The fixed phase relation between the branched waves is not needed by measurement of luminescence.

In WO92/19976, R. Kunz has described the device which includes two or more integral-type measurement strips for detection (detection of the bad smell especially by artificial nose) of the compounded signal.

Substantially for a luminescence detecting method, use of the planate minerals waveguide of a single mode was only comprehensively described in conventional technology, and explanation of the concrete requirements about excitation and detection of luminescence is not performed. In particular the range or abnormal-conditions depth of the good layer thickness which is, can carry out and can obtain a very good result is not shown.

It is known that the sensor platform which used at least two planes, the independence, and the inorganic dielectric waveguide field on a common substrate as the base will be producible by a simple method. This platform is suitable for parallel dissipation excitation and detection of luminescence in the same or different quality of an analysis target subject. Those independent waveguide fields are provided with one or more joint gratings, respectively.

I hear that the advantage with this big sensor platform can detect some sample solutions simultaneously by high sensitivity, for example, and there is. Washing between each measurement or a cleaning process is unnecessary, and, as a result, the amount of sample treatment per unit time becomes high. This is dramatically important [about everyday analysis or analysis of the gene engineering field] especially.

In addition to simultaneous analysis of two or more sample solutions, the one sample solution can also be continuously examined simultaneous on one sensor platform on some of the quality of an analysis target subject. This is advantageous especially when it is the examination of blood or a blood serum which can be carried out especially promptly and economically.

When analyzing some sample solutions simultaneously, and a waveguide field is independently, the cross talk between the luminescence signals from a different sample is prevented.
High selectivity and a low error rate are realized by this method.
Since a waveguide field is independently, it is possible to raise selectivity and sensitivity further by using it [for the purpose of the light source in which wavelength differs].
I hear that the further advantage of said sensor platform can use each independent waveguide field for optical, chemical, or a fluid engineering target, choosing it, and there is.
Especially the sensor platform provided with the planate waveguide field where the mode of only one or a small number is guided and which became independent physically or optically is suitable. Such a sensor platform is especially characterized by high sensitivity and very small composition. Generally, sensitivity of this level is not realized by the multimode waveguide constituted planate.
Excitation light can be entered using a lens, prism, or a grating, or the end face of a waveguide can be made to carry out direct entering.
Generally the incidence using a grating and the outgoing radiation in a suitable case are simpler than the case where a lens or prism is used, and more efficient. As a result, the intensity of the light wave which entered also becomes larger. This combines with the extinction ratio of the guided light wave being low, and brings about height with extraordinary sensitivity in this composition.
By using the most powerful possible EBANESSENTOFIRUDO, sensitivity can be raised further. This becomes possible to measure also about very little photogene on the surface of a waveguide.
The objects of this invention are a substrate of the continuous permeability, and a sensor platform which includes a plane and an inorganic dielectric waveguide by permeability, a) The plane and the inorganic dielectric waveguide are divided into at least two waveguide fields in the measurement region at least by said permeability, It is divided by the fact that the effective refractive index of the field where a wave is guided is larger than the field of the circumference, or division of a waveguide is performed by the substance on the surface which absorbs incident light. ;
b) Said waveguide field is provided with one incidence grating or a common

incidence grating, respectively so that it may be maintained after the propagating direction of a wave vector entering. ;
c) It is a sensor platform which is characterized by providing said waveguide field with one outgoing radiation grating or a common outgoing radiation grating, respectively in a suitable case.
This invention does not include the composition by two waveguide fields which join after branching in the shape of a Y character first, for example in both ends. The reason is for changing in that case, after the propagating direction of a wave vector entering. Such composition is a known thing. For example, it is used as an interferometer.

In this invention, the purpose of a waveguide field of having become independent is to provide the sensor platform for carrying out simultaneous detection of the luminescence excited in dissipation from one or more quality of an analysis target subject.
The words and phrases a "test section" and a "measurement region" are used as a thing of homonymy in the context of this invention.
The independent outside of a waveguide field itself can be chosen arbitrarily. If this outside is determined based on the composition of the overall device with which a sensor platform is attached, it is advantageous. The example of this outside is a straight line, a strip, a rectangle, a circle, an ellipse, a chessboard pattern, a rhombus, a honeycomb pattern, or an irregular mosaic. The dividing part between each waveguide fields is a straight line intrinsically. These dividing parts may arrive at both ends, and, on the whole, may be larger than a measurement region, or may be narrow.
Said waveguide field is preferably arranged by the shape of a strip, a rectangle, a circle, an ellipse, and a chessboard pattern.
Said waveguide field is especially arranged by parallel strip shape.
A still more suitable example arranges said waveguide field in the parallel strip shape joined at an end or both ends, and is acquired by maintaining the propagating direction of a wave vector eternally, even after entering.
Said strip joins in one end and another advantageous example is opened by the other end.
As [be / still / even after the propagating direction of a wave vector entering / eternal].

2 d of feasibility high composition [some of] is shown more from 1d and 2a from drawing 1 a.
: which shows the following [reference mark / each] -- waveguide; added to 1 board
2 Field formed by the absorbent material on the surface of a waveguide, or reduction (what provides an opening instead of a waveguide as simplest method) of the effective refractive index in the flat surface of a layer; 3 and 3' -- respectively -- incidence and an outgoing radiation grating.
The waveguide field (measurement region) is interrupted for drawing 1 a by the partitioning region. Those partitioning regions do not contact a connection element.
In drawing 1 b, the incidence grating common to all the measurement regions and the outgoing radiation grating exist. There is no contact with a partitioning region.
In drawing 1 c, the partitioning region has extended exceeding the connection element. However, the incidence in a waveguide field is not influenced by that.
Although drawing 1 d includes two joint gratings, other points are in agreement with drawing 1 c.
2 d of joint gratings do not continue from drawing 2 a, but each waveguide field shows the composition which has a grating individually.
The waveguide field which became independent physically or optically is producible by a known method. Two fundamental methods are feasible. For example, after producing the layer which dissociated from the beginning physically with the vacuum deposition using a mask, and formed the layer or of which b continuation was done, it constitutes using a suitable method.
As an example of the method a, there is vacuum evaporation of an inorganic waveguide material using the mask which covers a part of sensor platform and which was constituted appropriately. Such a mask is a known thing in manufacture of an integrated circuit. It is necessary to carry out direct contact of these masks to a sensor platform. The mask of a positive or a negative can be used.
applying the suspension of an inorganic waveguide material to a sensor platform through the mask constituted appropriately -- sol -- it is also possible to form a waveguide by gel art.

The independent waveguide field is formed by this method, and that division is performed by the opening in the easiest example. This opening can be filled with another material whose refractive index is lower than a waveguide after that. When division into some waveguide fields is performed by this method, the difference of the effective refractive index between the materials contiguous to a waveguide field exceeds 0.2 unit preferably, and exceeds 0.6 unit preferably especially.

As an example of the method b, the layer which continued by vacuum evaporation of an inorganic waveguide material is formed, and there are some which divide this layer into each waveguide field after that by mechanical scratching, material processing by laser, lithography processing, or plasma etching.

Generally this vacuum evaporation is carried out by a vacua. Plasma deposition is possible similarly.

It is necessary to make reference specially about processing using pulse-ized excimer laser and solid state laser, or a continuous gas laser. In the case of pulse-ized high energy laser, this composition can be broadly carried out via a mask. In the case of the laser which operates continuously, on the whole, the beam which converged passes the waveguide constituted, or a waveguide moves to a beam.

A suitable lithography processing method is the etching technology which is used for manufacture of a printed circuit board or micro electronic parts. By these methods, the precision of the composition from the range of very various geometrical patterns and the micrometer or the range of less than the micrometer becomes realizable.

In the case of an ablation processing method, a waveguide is removed selectively or thoroughly, but not being divided is completely important for a sensor platform. When an interlayer exists, it can remove completely selectively in a similar manner.

In modification of the method b, the layer which an inorganic waveguide material followed is added first, and composition is performed in the layer by the method that a waveguide field is divided by the absorption area, i.e., the field not guiding waves, in the 2nd phase using the absorbent material which interrupts a waveguide after that.

This absorbent material can be used as an inorganic material like metal with high optical absorption coefficients, such as gold, silver, chromium,

and nickel, for example, organic compounds, such as a polymer dyed and colored. Such materials can be added to a waveguide in the form of colloid solution like [in the case of the continuous layer or metal]. Selection of an option is also possible.

The deposition method for the composition carried out by a vacua is already mentioned in the above.

The colloidal matter in water or organic solvents, such as underwater gold, can be similarly used for waveguide field composition.

adhesion of gold of the colloid to the surface by spontaneous "set" -- R. It is described by Griffith and others (R. Griffith et al.) ("science (Science)" 1629 - 1632 pages of volume [267th] (1995)). For example, the layer diversion of river which the golden colloidal solution was physical or was divided into the fluid engineering target may be made to flow on a waveguide, and golden particles may be made to adhere to the shape of a strip. If the surface is dried, the independent waveguide field by this invention will be obtained. In order to perform desirable absorption, colloid of adhering gold must have a size of 10 thru/or 15 nm at the minimum. The diameter of this colloid is 15 thru/or 35 nm preferably.

Adhesion of gold of colloid can be carried out also by Stamping to the surface. Stamping of dissolved organic materials is described by white size (Whitesides) as "micro contact printing (microcontact printing)."

since the golden surface is constituted using a fluid alkane thiol, it is used (J. -- L. Wilbur Adv(s) (J. L. Wilbur et al.). Mater. 6th volume 600 -604-page (1994); -- Y. Xia (Xia) and G. M. white size.) J. Am. Chem. Soc. -- 3274 - 3275 pages of volume [117th] (1995).

For example, that configuration pattern can be transferred on the waveguide surface by attracting a golden colloidal solution in the stamp made from the elastomer which has a desired configuration pattern, and making this stamp contact.

Flexibility can use very highly the method of using an organic solvent or water easily when using it. A waveguide can be constituted by these methods just before implementation of luminescence assay.

It is necessary to embellish the waveguide surface so that a colloidal particle and the waveguide surface may adhere good, for example before colloid adhesion of gold depending on the case. This adhesion is realized by a canal interaction, foundation RUWARUSUKA, a dipole-dipole interaction,

a simple electrostatic interaction, or the covalent bond. This interaction is brought about by functionalization on colloid and/or the surface of a waveguide.
The suitable method of surface ornamentation and realization adhesion, For example, the 6th volume of "an ADOVANSHIZU yne colloid and interface science (Advances in Colloid and Interface Science)", L. They are BOKUSANI (Boks wart yi), O. Reardon (Liardon) and E. KOVATSU (Kov**s), and silanizing that is described by 95 - 137 pages (1976). Such silanizing is used also in order to improve adhesion of the recognizing element in affinity sensing.
Especially (mercaptomethyl) mercapto end Silang, such as a dimethylethoxy silane, is suitable for bringing about adhesion of gold by formation of a sulfur-gold covalent bond.
In the 2nd step, by being in making the same inorganic material as the layer which minerals waveguide material followed adhere to the form of a certain composition, and as a result increasing layer thickness, increase of an effective refractive index is brought about and, thereby, propagation in light wave mode concentrates another modification of the method b on a consequential measurement region. Such a "slab waveguide" and its producing method, "semiconductor integrated optics introduction (Introductionto Semiconductor Integrated Optics)
" (ATEKKU house company (Artech House Inc.) (1995)) -- setting -- H.P. It is described by ZAPPE (Zappe).
The strip width of these waveguides is 5 micrometers thru/or 5 millimeters preferably.
They are 50 micrometers thru/or 1 millimeter especially preferably.

If the width of a waveguide field becomes narrow too much, an available sensor area will also become small. If strip width and a required sensor area conform mutually, they are advantageous.
Each size and width of a waveguide field can be changed broadly, and they are substantially dependent on the composition of the use and the overall system which were meant.
When a waveguide field is strip shape, the length of each waveguide field is 0.5 thru/or 50 mm preferably, is 1 thru/or 20 mm especially preferably, and is 2 thru/or 10 mm still more preferably.
The number of the strips on a sensor platform is 2 thru/or 1000 preferably.

It is 2 thru/or 100 especially preferably.

each waveguide field -- as the strip for example, on a substrate -- each class -- even if small, it can divide into 2 or more sets which consists of two strips, and can arrange, and a multiplex detection area can be formed. The big practical advantage of the multiplex detection area assembled in this way, It is not necessary to perform cleaning of a sensor platform, or exchange between the measurement which much quality of an analysis target subject followed, what is necessary is just to make me hear that a sensor platform is displaced to an excitation device, a fluidics device, and a sensing device, and it is.

I hear that such a multiplex detection area can be produced more economically, and it has the further advantage. I hear that the separation at the divided sensor platform which time is taken dramatically and expense concentrates is unnecessary for a very big advantage, and it has it.

Each multiplex detection area comprises preferably 2 thru/or 50, and a waveguide field in which 2 thru/or 20 became independent preferably especially.

a sensor platform top -- desirable -- 2 thru/or 100 -- the multiplex detection area of 5 thru/or 50 exists preferably especially.

The feasible composition of the sensor platform provided with two or more multiplex detection areas is shown in drawing 3 a and 3b.

It is possible to produce by press forming by the method same with the substrate being provided with disk form and used for the present compact disk.

it can be come out of whole construction with the fluidics disk which includes the disk-like sensor platform provided with two or more multiplex detection areas, and a fluid supply way and actual cell space, and it can be constituted. Two parts are joined by adhesion and a unit is formed. However, square well-like cell space can also be alternatively formed in a disk-like sensor platform. Such an example is covered with a planate lid after that.

It is as having defined the reference marks 1-3 above, and 4 shows a certain whole multiplex detection area, and 5 is a substrate. 6 is a central notch which can accommodate an axis in order to pass each multiplex detection area 4 under the optical apparatus for excitation and detection by rotation.

The entrance and outlet opening part for the solution which is needed during assay in 7 and 7 are shown.
Generally those solutions are contacted to the recognizing element fixed on the waveguide field via a flowing-through cell with at least two openings.

A multiplex detection area may be alternatively arranged to concentric circle shape. The next multiplex detection area seems to be located under the optical apparatus for excitation and detection, if the distance between each multiplex detection areas is rotated at the angle of 5 thru/or 20 degrees.
Drawing 4 a and b shows a similar structure of the sensor platform on a disk.
As compared with drawing 3, not a tangential direction but the difference of being arranged radiately has each multiplex detection area 4, and, thereby, use of surface area is improved.

Another composition is shown in drawing 5 a and 5b. Each multiplex detection area 4 is arranged by rectangular chessboard pattern state. However, a multiplex detection area can also be arranged like each picture in filmstrip. This filmstrip is made into a planate element, or may be rolled round. Each multiplex detection area can be transported under the optical apparatus for excitation and detection by a method similar to a film. Also in the case of a multiplex detection area, the suitable composition shown about said independent waveguide field is applied.
The sensor platform which made this invention the background is a self-support type element which can be constituted in the geometry of a strip, a plate, and other requests [a disk and]. This sensor platform is intrinsically planate. The selected geometry is not deterministically important in itself, and it can be chosen so that the structure of the whole device where a sensor platform is attached may be suited. However, a sensor platform can also be used as an independent element which became independent physically [the excitation light source and a photoelectron optical detection system]. Composition which enables a substantial miniaturization is preferred.
A suitable substrate is the glass or quartz of all the kinds, for example. The glass in which optical processing of etching, grinding, polish, etc.

is possible the simplest is used small [the grade of the luminescence with it]. [desirable as much as possible] [a low and optical refractive index and] [most peculiar possible] This substrate has permeability about the wavelength of excitation and radiation preferably at least. Microscopic granularity of the substrate should be made as small as possible.
For example, EP-A-0 533 Penetrable thermoplastics which is described by 074 can also be used as a substrate.
A refractive index is below the refractive index of a substrate, and thickness can also cover a substrate by a film of 0.01 mm or less. In order that this layer may prevent fluorescence excitation within an inconvenient substrate and may reduce the surface roughness of a substrate, it is used, and it can consist of inorganic materials, such as thermoplastics, a plastic over which the bridge could be constructed over with heat or was constructed by the structure target, or SiO_2.
a refractive index is lower than a waveguide -- the penetration depth of EBANESSENTOFIRUDO -- thickness -- a considerable grade, when a large (that is, large farther than 100 nm) interlayer exists, If excitation light is emitted from the upper surface of a sensor platform, the permeability of only this interlayer about the wavelength of excitation and radiation is enough. In this case, a substrate can be made into the thing of absorptivity. Especially it comprises penetrable thermoplastics, a desirable substrate material is polycarbonate, polyimide, or poly methyl methacrylate.
It is preferred that a refractive index is the same about all the waveguides. That is, all the waveguides are formed with the same desirable material. The refractive index of a waveguide must be larger than the refractive index of a substrate, and an interlayer's refractive index used. A planate penetrable waveguide comprises a desirable material with a larger refractive index than 2.
For example, as a suitable inorganic material, especially an inorganic metal oxide, there are TiO_2, ZnO, Nb_2O_5, Ta_2O_5, HfO_2, ZrO_2, etc.
Ta_2O_5 and TiO_2 are preferred.
The thickness of a waveguide is 40 thru/or 1000 nm preferably.
It is 40 thru/or 300 nm especially preferably, and is 40 thru/or 160 nm still more preferably.

In a certain suitable example, the thickness of a waveguide is the same.

The abnormal-conditions depth of a grating is 3 thru/or 60 nm preferably. It is 3 thru/or 30 nm especially preferably.

The ratio of abnormal-conditions depth to layer thickness is 0.5 or less preferably.
It is 0.2 or less especially preferably.

the grating for incidence of excitation light, or the grating for outgoing radiation of the recombined luminescence light -- an optical diffraction grating -- it has the shape of a relief grating preferably. This relief structure can take various shape.
The composition of a sinusoid, a rectangle, a sawtooth wave, etc. is suitable. The method of producing such a grating is a known thing. About those production, the method and etching technology by the photolithography or a holography are used in many cases, They are described by "the chemical biochemical and ENVAIRON mental phi BASEN cers V", Proc. SPIE, the 2068th volume, and 313 - 325 pages (1994). The method according to molding or Stamping about the substrate of an organic matter is also available.
After forming the structure of said grating on a substrate, it transfers to a waveguide, and the grating structure reproduces self there, or a grating is formed into the waveguide itself.
The cycle of said grating can be 200 thru/or 1000 nm, and its grating is advantageous in it being single diffractive namely, suddenly also only about one periodicity. As for the grating cycles chosen, it is preferred that it is the thing that excitation light is combined in primary diffraction.
As for the abnormal-conditions depth of said grating, it is preferred that it is the same size.
The bar versus space ratios of said grating are 0.5 thru/or 2 preferably. It should be understood that a "bar versus space ratio" is a ratio of the width of a bar to that of space, for example in the case of a rectangular grating.
Said grating can be used also in order to make the luminescence light recombined with the waveguide also in order to enter excitation light in each waveguide emit.
About analysis of the sample from which luminescence differs, when all or

a part of grating constants of the incidence grating and the outgoing radiation grating differ, there is an advantageous thing.
In a certain suitable example, the grating constant is the same about all the gratings.
As for the grating constant of an incidence grating, when it is used for incidence of a part of grating of light and another part is used for outgoing radiation of light, it is preferred to differ from the grating constant of an outgoing radiation grating.
The intervals of said grating are B<=3and$X_{1/e}$ preferably, and $X_{1/e}$ is the distance to which intensity I_0 of the guided radiation fell to I_0/e.
The plane and the inorganic dielectric waveguide field are mutually classified along with the test section by the change in at least 0.6 of a refractive index at least by the permeability on :sensor platform in the category of an example with said preferred sensor platform.
. [whether each field is provided with one piece or two independent grating couplers, and] Or it has one piece or two common grating couplers in all the whole field, and the ratio [as opposed to / field / a plane and / inorganic / dielectric waveguide / thickness / 3 thru/or 60 nm and thickness in 40 thru/or 160 nm and the abnormal-conditions depth of a grating] of abnormal-conditions depth is 0.5 or less in said permeability.

The simplest method of bringing about 0.6 or more changes in a refractive index is dividing a waveguide thoroughly, and making an opening include, or making water include selectively during measurement.
Said waveguide guides only one thru/or the three modes preferably, and they are single mode waveguides especially preferably.
The further object of this invention is the sensor platform which changed, wherein one or more specific binding partners as a chemical or biochemical recognizing element about one or more same or different quality of an analysis target subject are fixed on the surface of a waveguide field.
Being able to add various specific binding partners to the surface of a waveguide field, those physical separation in each waveguide field is not important. They may exist, for example as a random mixture. Then, it is advantageous when the quality of an analysis target subject from which a radiation wavelength differs is simultaneously measured via an outgoing radiation grating.

The specific binding partner can fix at various places on a waveguide field according to the photochemical bridge construction which is described by WO94/27137, for example. Another method trickles the specific binding partner fixed by the head section of a multiple pipette, and adds him. This method can also be enforced using the ink jet printhead provided with the electrostrictive actuator which changed. This method can be enforced promptly and it has the advantage of ending with very little use. This is a precondition about formation of the geometrical patterns in which a thin strip or others were constituted precisely.

Another [in which the operation for dissociating physically on a waveguide field and fixing a specific binding partner is very easy] suitable method is based on use of a flow cell.

In the case of laminar flow, this separation can be mechanically carried out within a flow cell on a fluid engineering target in the form of a division bar.

In this method, the geometric arrangement of the diversion of river which supplies a bonding partner is substantially in agreement with arrangement of the waveguide field on a sensor platform. Especially when this fixing method using a flow cell embeds a specific binding partner in a fluid medium like [in the case of a lipid-film boundary receptor] in stable environment, for example, it is advantageous.

The specific binding partner who did the covalent bond to golden colloid can be made to adhere by the same method as formation of the field described [especially] above by this method not guiding waves. Especially in order to guide waves in a fixed field, it is necessary to use less than 10 nm of colloid of gold with a very small diameter below 5 nm.

Another easy method of operation is based the same on Stamping to the surface by the specific binding partner who combined with the specific binding partner or metal in the method similar to formation of the above-mentioned field not guiding waves.

Suitable metal is gold.

The suitable pattern which became independent physically is a pattern of a strip, a rectangle, a circle, an ellipse, or a chessboard.

The changed sensor platform, wherein a specific binding partner is stationed only one sort on the surface of each waveguide field is preferred.

Another suitable example of the sensor platform which changed is acquired

when the adhesion promotion layer is located between a waveguide field and the fixed specific binding partner.
50 nm or less of this adhesion promotion layer thickness is less than 20 nm especially preferably preferably.
Whether it is based on photochemical activation, a multiple pipette head, It is possible to add an adhesion promotion layer only to a waveguide field selectively using the wet chemical methods, such as Stamping of an ink-jet printer, the flow cell [mechanical or] accompanied by flow engineering separation of a flow, colloid adhesion, and the surface, or to passivate in the field not guiding waves. These methods are already described above about direct immobilization of the specific recognition element to the surface embellished or functionalized chemically arbitrarily.
It is direct, or by the selective immobilization only to the waveguide field of the specific recognition element by an adhesion promotion layer, since nonspecific combination of the quality of an analysis target subject in the field which is not used for signal generation decreases when using a wrap sample cell, the sensitivity of a detecting method increases both a waveguide field and the field not guiding waves.
The above-mentioned suitable composition about a sensor platform is applied also like said sensor platform which changed.
Said sensor platform which changed is completely [preferably] selectively refreshable, and the use covering several times is possible for it. An affinity complex can be made to dissociate selectively under relevant conditions, for example, low pH, an elevated temperature, use of an organic solvent, and so-called use [of a chaotropic agent (salt)] **, without spoiling the binding capacity of the fixed recognizing element substantially. It depends for detailed conditions on each affinity system greatly.
The concrete method of the luminescence detection in assay makes main elements immobilization of the luminescent substance used for detection of the direct quality of an analysis target subject on the waveguide field surface.
These substances can be used as two or more photogens which are excited, for example on the waveguide field surface, and can emit luminescence and which were combined with protein. If the partner who has compatibility to protein passes this fixed layer, luminescence will change by that cause

and the determination of the quantity of the partner who has compatibility of it will be attained. It is also possible to carry out the sign of the partner of the both sides of an affinity complex with a photogen, for example, to determine concentration especially, based on the energy transfer between the both sides accompanied by the optical quenching of luminescence.
One suitable fixing method which will be accepted for chemical or biochemical affinity assay fixes the quality of an analysis target subject itself, or one or more specific binding partners as a chemical or biochemical recognizing element to one of the bonding partners on the sensor platform surface. In [these assays are constituted in one or more stages, and] those stages, One or more solutions containing the specific binding partner to the recognizing element fixed on the sensor platform surface can be passed as a step which continued on the sensor platform surface, and the quality of an analysis target subject is combined in one of the partial steps of these. Such quality of an analysis target subject is detected by participant combination by which the luminescence sign was carried out in affinity assay. The substance by which the luminescence sign was carried out may be any one or more of the bonding partners in affinity assay, or may be an analog of the quality of an analysis target subject which has a photogen. I hear that existence of the quality of an analysis target subject needs to bring about a luminescence signal selectively, or needs to bring about change of a luminescence signal selectively, and the only precondition has it.
Since the sensor surface of activity is expanded chemically, a chemical or biochemical recognizing element is also fixable by a suitable method in what is called the particles in which immobilization of a up to [a sensor platform] is possible, and a "bead." The necessary condition for using the bead which can constitute the substance in which plastics etc. differ is that an interaction with the quality of an analysis target subject advances to an effective grade within the penetration depth of EBANESSENTOFIRUDO in the first place.
It is not receiving interference whose waveguide characteristic is [second] serious.

In principle, a recognizing element can be directly fixed on a waveguide field by for example, canal adsorption or a covalent bond, or can be fixed

by silanizing or addition of a polymer layer after surface chemical modification. Since direct immobilization of a up to [the waveguide of a recognizing element] is made easy, it is possible to add the thin interlayer who comprises SiO_2, for example as an adhesion promotion layer. Silanizing of glass and a surface of metal is comprehensively described by articles, such as the 6th volume (L. BOKUSANI, O. Reardon and E. KOVATSU, 95 - 137 pages (1976)) of a "ADOVANSHIZU yne colloid and interface science" etc., for example. The fixed concretely feasible method is already described above.

Binding protein to an antibody [as opposed to / for example / an antigen in a suitable recognizing element], and an immunoglobulin, such as protein A and G, The chelating agent [biological and] to histidine marker components, such as a chemical receptor and protein by which the histidine sign was carried out, to ligand, It is the lectin to the enzyme, the enzyme cofactor or enzyme inhibitor, and carbohydrate to the avidin and the enzyme substrate to the oligonucleotide and the single strand of RNA or DNA, and biotin to a complementary strand, etc. It is dependent on the composition of assay which is fixed by the sensor platform surface among suitable affinity partners. A recognizing element may consist in a nature, and may be manufactured or compounded by gene engineering or bionics.

The words and phrases a "recognizing element" and a "specific binding partner" are used as a thing showing the same meaning.

The above assay itself may be any of multi stage story methods, such as the single step complexing methods, such as a competitive measuring method, or sandwiches assay.

The easiest example of a competitive measuring method contacts the sample which includes the compound of the same known amount on the sensor platform surface except the luminescence sign being carried out to the quality of an analysis target subject with strange concentration, Then, the molecule by which the luminescence sign was carried out, and the molecule by which a sign is not carried out compete about the binding site on those fixed recognizing elements. In the composition of this assay, when the sample does not contain the quality of an analysis target subject, the greatest luminescence signal is acquired. An observable luminescence signal falls as the concentration of the substance which should be detected increases. In competitive immunoassay, the recognizing element fixed on the sensor

platform surface does not need to be an antibody, and may be an antigen. Generally, it is the problem of the selection in chemical or biochemical affinity assay which [of these partners] is fixed. This is one of the main advantages of assay based on luminescence over the methods of being based on change of the amount of adsorbates in EBANESSENTOFIRUDO of a waveguide field, such as surface plasmon resonance or an interferometry. The competition in the case of a competitive measuring method does not need to be limited to the thing about the binding site of the sensor platform surface. For example, the antigen of a known amount can be fixed on the sensor platform surface, and the sample which includes the same antigen and the antibody by which the luminescence sign was carried out of the unknown which should be detected as quality of an analysis target subject can be made to contact. In this case, the competition for combining with an antibody takes place between the antigen fixed by the surface and the antigen in a solution.

The easiest example of multi stage story assay is sandwiches immunoassay by which a primary antibody is fixed by the sensor platform surface. Combination of a second antibody which is used for combination of the antigen which should be detected, and the second epitope detection of an antigen and by which the luminescence sign was carried out, . [whether it carries out by continuous contact with the 2nd solution that includes the solution which includes an antigen, and the antibody by which the luminescence sign was carried out, and] Or it is possible to carry out, after mixing these two solutions beforehand so that the partial complex which consists of an antibody by which the luminescence sign was carried out to the antigen may be combined eventually.

Affinity assay may include a still more nearly additional connection step. For example, in the case of sandwiches immunoassay, in the 1st step, protein A is fixable on the sensor platform surface. This protein combines an immunoglobulin with what is called that Fc section specifically, and they act as a primary antibody in subsequent sandwiches assay feasible as mentioned above.

There are many methods in affinity assay at others, such as a thing using a known avidin biotin affinity system.

The example of the method of affinity assay is J.H. RITTEMBAGU (Rittenburg). "The principle of immunoassay (Fundamentals of Immunoassay)", "development

and application (Development and Application of Immunoassay for Food Analysis) of the immunoassay about food analysis" (J. -- the volume on H. RITTEMBAGU.) ERUSU veer (Elsevier), Essex (Essex) (1990), Or P. TISEN (Tijssen) "actual condition of enzyme immunoassay, and theoretical (Practice and Theory of Enzyme Immunoassays)" (R. and) [H. burden] P.H. It sees in the volume on Van NIPPEMBAGU (P. H. van Knippenberg), an ERUSU veer, and Amsterdam (Amsterdam) (1985).
The further object of this invention is the method of determining one or more luminescence in parallel using the sensor platform or the sensor platform which changed by this invention.
This method contacts one or more liquid samples to one or more waveguide fields on a sensor platform, Excitation light is made [entering excitation light in a waveguide field, and] to penetrate in a waveguide field, It includes exciting in EBANESSENTOFIRUDO the photogene fixed on the photogene in a sample, or a waveguide field by that cause in parallel, and measuring the luminescence which this generated using an optoelectronics device.

The above-mentioned suitable composition about a sensor platform and the sensor platform which changed is applied also to this method.
Only the parallel beam of light is substantially suitable for luminescence excitation. "It is substantially parallel" should be understood to mean emission of less than 5 times as used in the context of this invention. This means that the beam of light is radiating slightly, or it may be converging slightly. For luminescence excitation, use of coherent light is preferred, especially a 300 thru/or 1100-nm laser beam has preferred wavelength, 450 thru/or 850 nm is still more preferred, and 480 thru/or 700 nm is the most preferred.
The examples of usable laser are die laser, a gas laser, solid state laser, and a semiconductor laser. When required, a radiation wavelength can also be doubled with a nonlinear crystal optical apparatus. A beam can be converged further, or it can be made to be able to polarize using an optical element, or can also be made to decrease with a neutral gray filter. Especially the racer for which it was suitable is the argon / ion laser, and the helium/ion laser which emanates, respectively on the wavelength of 457 thru/or 514 nm and 543 thru/or 633 nm. Furthermore, the diode laser which made two times the diode laser or frequency made from the

semiconductor material which emanates with the fundamental wavelength of 630 thru/or 1100 nm is suitable.
This is because power consumption is low small again, so the substantial miniaturization of the whole sensor system of those sizes is attained.

It should be understood that a "sample" is the whole solution which may include the substance of an analysis target subject which should be detected, i.e., quality, in the context of this invention and which should be analyzed. This detection is feasible and is contacted in one or more solutions to the surface of a sensor platform during this assay by assay of a single step or a multi stage story.
At least one of the solutions used includes photogene detectable according to this invention.
When photogene has already adsorbed on the waveguide field, the sample does not need to contain luminescent components. This sample may contain further ingredients, such as pH buffer solution, a salt, acid, a base, a surface-active agent, a viscous adjustment additive agent, and a color. In particular, a physiological salt solution can be used as a solvent. Addition of a solvent can be omitted when luminescent components are fluids in itself. In this case, it is possible to make content of the photogene in a sample 100%.
Samples may be biological media, such as an egg yolk, body fluid or its ingredient especially blood, a blood serum, plasma, and urine. It may be the alcohol or synthetic sake by the extract solution and a biological process from the medium by nature or composition, such as the surface water of aggregate, the ground, and vegetable [some].
A sample may be used with the solvent which could use it, without diluting or was added.
Suitable solvents are water, an aqueous buffer, a protein solution, and an organic solvent. Suitable organic solvents are alcohol, ketone, ester, and aliphatic series carbohydrate. Use of the mixture of water, an aqueous buffer or water, and the organic solvent of miscibility is preferred. However, a sample may include the ingredient which does not dissolve in solvents, such as oligomer or a polymer by paints particles, a dispersing agent, nature, and composition. In this case, a sample serves as opaque distribution or emulsion optically.

The functionalized luminescence color which has the wavelength of luminescence in the range of 330 thru/or 1000 nm as a luminescent compound, For example, a rhodamine, a fluorescein derivative, a coumarin derivative, JISUCHIRI kana phenyl, a stilbene derivative, phthalocyanine, naphthalocyanine, poly pyridyl / ruthenium complex (a tris (2,2'-bipyridyl) ruthenium chloride.) A tris (1,10-phenanthroline) ruthenium chloride, a tris (4,7-diphenyl-1,10-phenanthroline) ruthenium chloride, Platinum/porphyrin complexes, such as poly pyridyl / phenazine / ruthenium complex, perpetuity europiums (octaethyl-platinum-porphyrin etc.) and a terbium complex, cyanine dye, etc. can be used. The color which has an absorption wavelength and a radiation wavelength in the range of 600 thru/or 900 nm is suitable for especially analysis of blood or a blood serum.
Furthermore colors, such as a fluorescein derivative, are suitable and it is a color containing the functional group which makes the covalent bond of the color possible.
For example, there are fluoresceinisothiocyanate etc.

Available functional fluorescent dye is commercially [Cy5.5 (registered trademark) color of monofunctional and two organic functions, etc. / from a biological detection systems company (Biological Detection Systems Inc.)] suitable in a similar manner, for example.
These are described by "Clinical Chemistry (Clinical Chemistry)" 40(9):1819-1822 page (1994).

Suitable luminescence is fluorescence.
When various fluorescent dye from which a radiation wavelength differs is used, and using especially an outgoing radiation grating, there is [although all can be excited by the light of the same wavelength,] an advantageous thing.
May combine the luminescence color used with one of the bonding partners in a polymer or a biochemical affinity system chemically, and these bonding partners' example, An antibody or an antibody fragment antigen, protein, peptide, receptors, or those ligands, They are binding protein, such as hormone or a hormone receptor, an oligonucleotide, a DNA strand and RNA chain, an analog of DNA or RNA, protein A, and G, avidin or biotin, an enzyme,

enzyme cofactor or enzyme inhibitor, lectin, or carbohydrate. It is reversible or irreversible (raw).

Use of the share luminescence sign which made reference at the end is suitable for chemical affinity assay. It is also possible to use the steroid, the lipid, and the chelating agent by which the luminescence sign was carried out. In the hybridization assay especially by a DNA strand or an oligonucleotide, it is suitable especially when an insertion luminescence color shows the luminescence especially reinforced like various ruthenium complexes when those colors were inserted. If those compounds by which the luminescence sign was carried out are contacted to the affinity partner fixed by the sensor platform surface, they can quantify those combination easily using the measured luminescence intensity. A fixed quantity of the quality of an analysis target subject can be performed by measuring change of the luminescence at the time of a sample interacting with a photogen in the form of enhancement of the luminescence which originates, for example in change of the optical quenching of the luminescence by oxygen, or proteinic conformation.

While the sample is standing it still, a waveguide field can be made to be able to contact, or a sample can be continuously passed on a waveguide field, and the circulation can be made intermittent in the method by this invention.

Another, important gestalt to which this method is applied is based on restricting generating of a signal in EBANESSENTOFIRUDO of a waveguide, when recombination is used also for signal detection in the first place. It is based on the reversibility of the complex formation by the affinity as a balanced process the second.

If a suitable flow is used in a flowing-through system, combination of the luminescence sign affinity partner in EBANESSENTOFIRUDO who joined together, or desorption, i.e., dissociation, can be followed in real-time. Therefore, this gentleman method is suitable for the kinetic research for determining various association constants or dissociation constants, or displacement analysis.

The luminescence excited in dissipation is detectable by a known method. Suitable things are detector arrays, such as a procession of a photo-diode, a photo cell, a photo-multiplier, a CCD camera, and CCD. Luminescence can be projected on said detector array by optical elements, such as a mirror,

prism, a lens, a Fresnel lens, and a graded index lens, and these elements can be arranged to each or seriate. Since a radiation wavelength is chosen, it is possible to use known elements, such as a filter, prism, a monochromator, a dichroic mirror, and a diffraction grating.

When the specific binding partner whom a large number became independent of physically relatively especially exists, it is advantageous to use the detector array arranged by the sensor platform latest. It is convenient if optical elements, such as a holographic filter for separating excitation light and luminescence light and an interference filter, are arranged between a sensor platform and a detector array.

The gestalt with this method detects the luminescence which was emitted isotropic and excited in dissipation.

In another gestalt of this method, the luminescence which was excited in dissipation and recombined in the waveguide field is detected via an outgoing radiation grating in a sensor platform edge. The intensity of this recombined luminescence is so high that it is unexpected, and, as a result, can obtain very good sensitivity using this procedure.

In another gestalt of this method, the both sides of the luminescence recombined in the luminescence which was excited in dissipation and emitted isotropic, and a waveguide are detected independently, however simultaneous mutually. Since the selectivity of these two luminescence detecting methods that are a function of the distance of a photogen and a waveguide field differs, if the method by this gestalt is used, the additional information about the physical distribution of a photogen can be acquired. It becomes possible to identify photochemical bleaching of a photogen, and dissociation of the affinity complex which supports a photogen.

Besides detection of luminescence, I hear that absorption of the emitted excitation light can also be measured simultaneously, and it has another advantage of this method. As compared with the multiplex-mode waveguide of the composition by fiber OPUTIKUSU or a flat surface, a good signal to noise ratio is obtained substantially in this case. The quenching effect of luminescence is detectable by high sensitivity by luminescence and the coincidence measurement of absorption.

This method can be carried out by performing excitation light radiation by operation of a continious wave (cw). That is, excitation is performed

for intensity using the light of a fixed place to time.
However, it is feasible also by this method's emitting excitation light as a timed pulse which has the pulse length from 1 pico second to 100 seconds, for example, setting the interval of a minute unit from a time resolving target or a second bit, when pulse length is short, and detecting luminescence. This method is advantageous, when the formation speed of combination should be pursued analytically, for example, or especially when exposure time should be prevented by shortening the fall of the luminescence signal resulting from photochemical bleaching. If suitable time resolving is performed about detection using the pulse length of moderate shortness, (In this case as much as possible durability) The scattered light of the luminescent components which are not desirable as for the sample which may exist by a tagged molecule's luminescence, or a sensor material, the Raman radiation, and distinction of temporary luminescence are attained. This is because radiation of the quality of an analysis target subject is detected only when temporary radiation declines. The excitation and detection after pulse excitation by which time resolving was carried out and which were luminescence-detected and were modulated enable it to investigate the influence of combination of the quality of an analysis target subject to the attenuation moving state of molecule luminescence. The damping time of molecule luminescence can be located in a line with recognition of the specific quality of an analysis target subject by the fixed recognizing element and physical limitation of the signal generation into EBANESSENTOFIRUDO of a waveguide, and can be used as a standard of the further selectivity.
This method can be enforced by emitting excitation light on one or more frequency with an intensity modulation method, and detecting the consequential phase shift and abnormal conditions in luminescence of a sample.
: which can carry out parallel incidence of the excitation light into two or more waveguide fields by some methods -- or [using the laser light source of a plurality] --;
b) Or [covering two or more waveguide fields and incidence gratings by extending the beam from a laser light source with a known suitable optical apparatus];
c) Divide the beam from a laser light source into two or more individual

beams using a diffraction element or a holography optical element, and enter those beams in a waveguide field via a grating, or use the arrangement of; or d solid state laser.
An advantageous procedure is realized by using the conoscope in which control usable in order to perform the incidence or outgoing radiation about a waveguide field with a time lag is free. As an option, a sensor platform can also be displaced appropriately.
Another suitable method excites luminescence by a laser light source with same or different various wavelength.
It is preferred to use the diode laser (laser array) of a single tier for luminescence excitation. Those parts can be very small, and it can manufacture economically, and has the special advantage that each laser diode can control individually.
Also in the case of the detecting method by fluorescence, the suitable composition described about the sensor platform is applied.
Drawing 6 is a diagram showing feasible whole construction. The reference marks 1 and 3 are as having given the definition above, : which is as follows [reference marks / other] -- the optical element for the optical element 14 detection for 8 sensor platform 9 filter 10 seal 11 flowing-through cell 12 sample space 13 excitation / electronic device For example, the excitation light from the diode laser 13 via the 1st grating 3. It is entered in the waveguide field 1 of the sensor platform 8. The flowing-through cell 11 is in the sensor platform 8 bottom, and is closely pressed to the sensor platform. A solution required for assay is made to carry out conduction of the space 12 in the flowing-through cell 11 which has one or more inlet openings and one or more outlet opening parts. In a waveguide field, a bonding partner's fluorescence is recombined in dissipation, is emitted to the detector 14 via 2nd grating 3', and is detected in the detector 14. The filter 9 acts so that the scattered light may be ****(ed) and removed.
Since preferably analyzes samples, such as an egg yolk, blood, a blood serum, plasma, or urine, this method is used.
Another suitable method is obtained in analysis of samples, such as alcohol by the surface water of aggregate, soil or a vegetable extract, the biological process, or a synthetic process.
This invention is related also to use of the sensor platform by this invention or the sensor platform which changed for a fixed quantity of the

biological substance in affinity sensing.
Since generating and detection of a signal are limited to the chemical or biochemical recognition surface of a waveguide and the disturbance signal from a medium is identified, combination of the substance to the fixed recognizing element can be pursued in real time. Therefore, it is also possible to use the method by this invention in affinity screening or displacement analysis, especially medicine development by direct measurement of the meeting speed in a flowing-through system by a suitable flow and a dissociation speed.
Use of the sensor platform by this invention for a fixed quantity [this invention] of a antibody or an antigen, or the sensor platform which changed;
b) A receptor or ligand, an oligonucleotide, a DNA strand, or RNA chain, Use of the sensor platform for a fixed quantity of the analog of DNA or RNA, an enzyme, an enzyme substrate, enzyme cofactor or enzyme inhibitor, lectin, and carbohydrate, or the sensor platform which changed;
c) Include use and; of the sensor platform by this invention for an alternative fixed quantity of the luminescent components in an opaque fluid, or the sensor platform which changed optically.
Opaque fluids may be environmental analysis samples, such as body fluid, such as biological fluid, such as an egg yolk, blood, a blood serum, and plasma, and the surface water of aggregate, a dissolved soil extract, and a dissolved plant extract, optically, for example. A suitable thing is a reaction solution which is obtained, for example in manufacture of chemicals especially a dye solution, or a reaction solution of an optical brightener.
A suitable thing is the distribution and the preparation of all the kinds which are used, for example in a textile industry, and includes one or more luminescent components. Therefore, this method can be used also for a quality control.
Many following examples explain this invention.
In many following examples of all, the unit M of concentration shows a mol/l.
Example A: coat production polycarbonate (PC) board using a mask with TiO_2 by vacuum evaporation in example Aof production 1 vacuum evaporation of various sensor platforms (method: sputtering, evaporation rate:0.5A/second, thickness:150nm). The mask made from aluminum in which

six 0.6-mm-wide strips were cut at 30 mm in length is introduced into the latest of the substrate between a target and a substrate. Six waveguide fields (measurement region) created as a result have a parabolic edge section which has a uniform thickness of 150 nm in a 600-micrometer-wide center section.

Layer thickness is decreasing in the shape of a slant face on both sides (gradually).

The layer thickness in said center section is the largest, therefore since an effective refractive index becomes the highest in a center section, the entering laser beam is restricted in a waveguide field.

Example A2 Production by secondary division It is operated using a 193-nm ArF excimer laser. A rectangular laser beam is converged on the beam profile with a 200-micrometer length [in width] of 20 mm which doubled the focus on the sensor platform using a cylindrical lens. The sensor platform is provided with the Ta_2O_5 layer of the continuous 100-nm thickness. Ablation of the whole layer is carried out by the single laser pulse (10 ns) in the energy density which exceeds 1 J/cm^2.

Example A3 Production by secondary division It is operated using 488-nm Ar ion laser. Using a microscope lens (40 times), on a waveguide, a focus is doubled and a circular laser beam is converged to 4 micrometers in diameter. The sensor platform is provided with the Ta_2O_5 layer of the continuous 100-nm thickness, and is arranged on the positioning element (Newport (New Port)PM500) by which motor control was carried out. Under the continuous laser radiation, a platform is moved to a beam and a perpendicular direction at 100 mm/s. With the output of 700 mW, ablation of the whole waveguide is carried out in a focus, and this forms two independent waveguide fields.

Example A4 Production by addition of the constituted absorption enveloping layer by a vacuum method The parallel strip of five sheets with stratified chromium/gold, the metallic-oxide (it continued) waveguide top which comprised Ta_2O_5 -- it carries out in 0.2nm/[in a second] by Cr, and vacuum deposition of the 45 nm is carried out for 5 nm of the beginning in 0.5nm/[in a second] by Au after that (vacuum evaporator: balzers (Balzers)BAK400). Incidence mode is interrupted by the absorption layer.

Example A5 The surface of the metallic-oxide (it continued) waveguide which comprised production Ta_2O_5 by addition of the constituted absorption

enveloping layer by an aquosity method is silanized by the dimethylethoxy silane in the 180 ** gaseous phase (mercaptomethyl). a fine pipette -- colloidal solution A (Ore Rion (Aurion) supplies -- and) [gold sol] The solution of average colloid 28.9 nm, and concentration:A_{520}**1 is added to the surface which was liquid drop-like, or made it the strip, and was embellished, and it incubates for 1 hour. [in diameter] The surface is washed with water after incubation. The part which had guided mode light incubated is made to absorb. A mode beam does not exist in the downstream of the part where it incubated any longer. Au colloidal solution B with which the same thing was covered by protein A (P-9785 which the sigma (Sigma) supplies, and the average diameter of 18.4 nm) It is applied to A_{520}**5.5 (glycerol 50%, 0.15M NaCl, 10mM sodium phosphate (pH 7.4), PEG20 0.02%, 0.02% of sodium azide). The absorption pattern on the waveguide surface is not spoiled after flashing of the abundance by water and ethanol. This shows the stability of composition of having been formed.

The continuous optical absorption strip can be formed by adding the micro drops (1microl) sequence of colloidal solution A by manual operation.

Example A6 The surface of the metallic-oxide (it continued) waveguide which comprised production TiO_2 by addition of the constituted absorption enveloping layer by an aquosity method is silanized by the dimethylethoxy silane in the 50 ** gaseous phase (mercaptomethyl). Then, a part of waveguide surface containing the front of the 2nd outgoing radiation grating, and the 2nd outgoing radiation grating. Colloidal solution B (P-9785 which the sigma (Sigma) supplies, and the average diameter of 18.4 nm) It incubates for 3 hours with A_{520}**5.5 (glycerol 50%, 0.15M NaCl, 10mM sodium phosphate (pH 7.4), PEG20 0.02%, 0.02% of sodium azide). The wave propagation in the part to which it incubated is intercepted thoroughly. The surface of the part where it incubated is investigated with an atomic force microscope, and the density of the gold grain required for existence of colloid and the optical absorption observed fixed to the surface is judged. The interval of an average of these particles is about 100 nm.

Example A7 The surface of the metallic-oxide (it continued) waveguide which comprised production Ta_2O_5 by addition of the constituted absorption enveloping layer by an aquosity method is silanized by a dimethylethoxy (mercaptomethyl) silane (180 ** gaseous phase). A waveguide chip is joined to the flowing-through cell accompanied by the layer diversion of river

divided into the parallel fluid engineering target. Here, individually, through the independent flow opening (1-5) in which an address is possible, contiguity parallel can be made to be able to carry out mutually along with the longitudinal direction on the surface of a waveguide, and the flow from which it differs to five by a fluid can be passed. The purpose is to produce three waveguide strips separated by two thinner strips by adhering Au colloid. A flowing-through cell is filled up with buffer solution (sodium chloride solution by which buffer processing was carried out by the phosphate (pH 7.0)) at the entrances 1, 3, and 5, and is filled up with Au colloidal solution at the entrances 2 and 4. The surface uses the colloidal solution blocked by bovine serum albumin (BSA gold marker (Gold Tracer) which Ore Rion supplies, average colloid 25 nm in diameter, OD_{520}**2.0). (every channel) The flow chosen is [styles / 1, 3, and 5 / buffer solution] a part for 0.05-ml/about two part colloid styles 2 and 4 for 0.167-ml/. As a result, as for the width of a colloid style, the width of about 1 mm and a buffer solution style is set to about 3 mm. Generally the ratio of the width of the colloid style to the width of a buffer solution style can be freely chosen via the ratio of a flow.

These flows are added for 20 (it is equivalent to the amount of colloid of 1 ml per channel) minutes. A waveguide chip is removed after the incubation for 20 minutes, and it washes with water, and is made to dry by nitrogen flow. Guided mode light is thoroughly absorbed by the strip fixed with colloid, and three independent optical guide modes about 3 mm wide are brought about.

The example B1 of example [of application] B: Two parallel detection B1.1 with the complementary strand fixed by two fields which became independent physically of a different oligonucleotide in hybridization assay by which the fluorescein sign was carried out. Are obtained by example A3.

photosensor platform size: with two waveguide fields -- 48 mm x 16 mmx0.5-mm waveguide: -- Ta_2O_5. n= 2.317 at 488 nm, the thickness 150**5-nm board:Corning glass (Corning Glass) C7059, n= 1.538 grating at 488 nm : A rectangular grating with an abnormal-conditions depth of 6-7 nm, grating-cycles: -- degree of incidence result bond angle: by excitation by 750-nm633 nm -- 4 degrees - 5 degrees (secondary diffraction) Incidence efficiency: In a grating position, it is 7% attenuation:2.5dB/cmB1.2. Optical design The excitation light from argon

ion laser (excited wavelengths of 488 nm) can extend to 10 mm using a cylindrical lens, It is turned on two gratings of a waveguide field from the back of a substrate in the mirror which can rotate freely. The flowing-through cell which is prolonged over two waveguide fields to a capacity of about 0.07 ml and which was controlled by the thermostat is pressed from the upper part to the upper surface of a waveguide, and the seal is carried out with the O ring. The luminescence of two samples excited in EBANESSENTOFIRUDO is simultaneously recorded by two detectors which became independent physically. The luminescence which these two detectors comprise a photo-diode (SR1133 HAMAMATSU (Hamamatsu)), respectively, and was emitted in cell space, While performing filtering using an interference filter, waves are guided on a photo-diode with the same glass optical fibre. These signals are amplified by two sets of trans impedance amplifiers. Each element used for this design is a known thing, and it is commercially available in it.

B1.3 Solution 10.069M phosphate buffer used (0.041M Na_2HPO_4+0.028M NaH_2PO_4) 0.176M KCL, 1 ml of POE-(20)-sorbitol mono- laurate (Tween (Tween)20, ICI), polyacrylic acid PAA5100 What prepared 1 g and sodium azide 500 mg/l to 1 l. with distilled water, and hybridization buffer solution (pH 7.75) come out of and constituted

2) The sample solution 1. (16xcfl) :. The oligomer fixed by the 1st waveguide field and 16 complementary base pairs. The oligomer 3 sample solution 2 (15xcfl) which comprises (fluorescein 5'-GTTGTGTGGAATTGTG-3' (10^{-8}M) in the hybridization buffer solution 1) and by which the fluorescein sign was carried out : to the 2nd waveguide field. The fixed oligomer and 15 complementary base pairs. The oligomer 4 reproduction solution which comprises (fluorescein 5'-TTTTTCTCTCTCTGT-3' (10^{-8}M) in the hybridization buffer solution 1) and by which the fluorescein sign was carried out : The solution of the solution above of urea 50% (weight ratio) KABURO. (Cavro) It is supplied with a pump (in each example, it is the amount of burets, and is 10 ml).

B1.4 Fixing method An oligonucleotide synthesizer unit (applied bio-systems (Applied Biosystems) 394B) is used, On the sensor platform silanized by 3-GURISHIJIROKI Cipro pill trimethoxysilane by the standard method in the oligonucleotide synthesis on particles, direct, A specific binding partner (the 1st waveguide field top 3' CAACACACCTTAACAC-the 5'

and 2nd waveguide field top 3' AAAAAGAGAGAGAGA) is compounded. However, a stable hexaethylene glycol linker is used for immobilization to the surface in the three-dash terminal of an oligonucleotide in contrast with a standard synthesizing method. The sensor platform which fixed the specific binding partner is washed with water, and it is used for assay after that.

B1.5 Measurement procedure The modification 1 (what makes two different quality of an analysis target subject get mixed up in time, and adds it simultaneously on two waveguide fields) of a measuring method performs washing for 2 minutes with : and the hybridization buffer solution 1 which comprises each following step (a part for 0.5-ml/), and records a background signal.;

- Add the sample solution 2 for 10 minutes (being a part for /5 ml after flashing during 5 seconds).; (a part for 0.5-ml/)
- Carry out Flushing during 2 minutes with the hybridization buffer solution 1.;
- Add the reproduction solution 4 for 3 minutes (a part for 0.5-ml/).;
- Carry out Flushing during 4 minutes with the hybridization buffer solution 1.;
- Add the sample solution 3 for 10 minutes (being a part for /5 ml after flashing during 5 seconds).; (a part for 0.5-ml/)
- Carry out Flushing during 2 minutes with the hybridization buffer solution 1.;
- Add the reproduction solution 4 for 3 minutes (a part for 0.5-ml/).;
- Carry out Flushing during 2 minutes with the hybridization buffer solution 1.

The entrance section arranged directly under a sensor platform condenses the fluorescence emitted isotropic from said two waveguide fields between said procedures with a rectangular (10 mm x 1 mm) light guide bundle. The rectangular cross section of these light guide bundles changes so that an exit may serve as a round shape (6 mm in diameter). An interference filter of the same kind to the downstream nearest to a light guide bundle exit (being 530 nm the transmissivity maximum, the bandwidth of 30 nm)

It *****. The fluorescence by which spectrum **** was carried out is measured with two photo-diodes. After adding the 16-mer complementarity sample by which the fluorescein sign was carried out for 10 minutes, a 42-mV

fluorescence signal is observed from the 1st waveguide field, and a signal is not observed from the 2nd waveguide field (1 mV). On the other hand, after adding the 15-mer complementarity sample by which the fluorescein sign was carried out for 10 minutes, a 43-mV fluorescence signal is measured in the 2nd waveguide field, and a signal is not measured in the 1st waveguide field (0 mV). A signal noise is about 2 mV.

The modification II (what adds simultaneously two different quality of an analysis target subject to two waveguide fields which became independent physically using the independent cell) of a measuring method, The hybridization buffer solution 1 performs washing for 2 minutes in the waveguide field of both :- that comprises each following step (a part for 0.5-ml/), and the background signal in both channels is recorded.;

- (A part for 5-ml/after flashing during 5 seconds) the sample solution 2 (a part for 0.5-ml/) -- the 1st waveguide field --; which adds the sample solution 3 (a part for 0.5-ml/) to the 2nd waveguide field for 10 minutes
- Carry out Flushing of the waveguide field for [both] 2 minutes with the hybridization buffer solution 1.;
- Add the reproduction solution 4 (a part for 0.5-ml/) to both waveguide fields for 3 minutes.;
- Carry out Flushing of the waveguide field for [both] 4 minutes with the hybridization buffer solution 1.

The entrance section arranged directly under a sensor platform condenses the fluorescence emitted isotropic from said two waveguide fields between said procedures with a rectangular (10 mm x 1 mm) light guide bundle. The rectangular cross section of these light guide bundles changes so that it may become a round shape (6 mm in diameter) at an exit. An interference filter of the same kind to the downstream nearest to a light guide bundle exit (being 530 nm the transmissivity maximum, the bandwidth of 30 nm) It ******. The fluorescence by which spectrum **** was carried out is measured with two photo-diodes. A clear signal is acquired from both waveguide fields.

Detection B2.1 of the recognizing element on an example B2:5 ** parallel strip The human antibody by which the sign was carried out by fixed Cy5.5 of the recognizing element, protein A, and BSA are fixed as a recognizing element and a contrast molecule in the strip of five fields of the sensor platform described by example A4.

The quality of an analysis target subject about all the recognizing elements is the Homo sapiens antibody by which the sign was carried out by Cy5.5 which shows the strip and affinity reaction of protein A.
All the strips are 0.6 mm x 15 mm, and the interval of a strip is 0.6 mm. The right direction starts [these strips] from a 1-mm position from the continuous incidence grating.
A multiplex channel cell with the following sizes is used for the immobilization which the recognizing element to a sensor platform surface top and the contrast molecule comprised. The six same channels as the size of the sensor platform for which the depth is used at 0.6 mm[in width] x15 mm in length are formed in the rectangular parallelepiped (size: 100mmx60mmx18mm) of Teflon. In the Teflon of the both ends of a channel, the drill hole is formed using a 0.6-mm drill.
Each channel is connected with from the Teflon block bottom.
With the shape as which the special shape of the channel formed in Teflon and the circumference of a channel were chosen, these channels are making the "lip" shape which projects about 0.2 mm from the dent for a waveguide. The waveguide which embellished the surface chemically by gaseous phase silanizing using 3-mercaptopropyl-dimethyl methoxysilane beforehand is arranged in the dent of a multiplex channel cell so that a waveguide may counter with a channel. By pressing a sensor platform to the lip of the Teflon of a multiplex channel cell, the joined part by which the seal was carried out is formed between the surface of a waveguide field, and a Teflon block. The following solutions are poured in into each channel via a drill hole.
Channel 1: The solution 1nM channel 2 of the Homo sapiens antibody by which Cy5.5 sign was carried out: Protein A-water 1mg [/ml] channel 3:BSA-water 10mg/ml channel 4:protein A - Do not do water 1mg [/ml] channel 5:protein A-water 1mg [/ml] channel 6:use of, but . After the incubation period of 2 hours, by pouring in demineralized water, a channel is washed and it dries by blowing nitrogen. The post sensor platform is removed from a multiplex channel cell, humidity of the waveguide surface is carried out with about 400micro of BSA solutions 1 with a concentration of 10mg/ml, and the activity binding site of the emainder on the silanizing surface is saturated with protein (BSA). BSA does not show compatibility to the Homo sapiens antibody which is used as quality of an analysis target subject and by which

Cy5.5 sign was carried out in this experiment. Demineralized water washes a sensor platform after the incubation period of 2 hours.

B2.2 Experiment composition for the automatic fluorometry about that bonding partner fixed by the recognizing element and the strip The composition of this measurement consists of the following three main elements.

A) The sensor platform provided with the flowing-through cell with which it united for the fluid contact of a waveguide field and various solutions sake, The flow cell of ********** which projects the strip field on the surface of a waveguide on a detector with the combination and mechanical screen of the optical apparatus C lens provided with the holding mechanism for the laser light source for forming the holding mechanism B excitation light beam which can be adjusted perpendicularly, and an optical element, On advancing side by side by which computer control was carried out, and a rotary unit, it is attached so that an incidence grating may be located in right above [of a rotary unit / axis-of-rotation]. Using an advancing-side-by-side unit, a flow cell can be located in accordance with this axis of rotation with a waveguide, and, thereby, the mode can be entered in the field of five molecule strips fixed by the waveguide.

This flow cell comprises fundamentally an aluminum plate whose size is 75mmx40mmx5mm, an O ring is inserted in that center, and the shallow chamber whose size is 28mmx6mmx0.2mm is formed by pressing a sensor platform to an O ring. Connection with this chamber is possible through three holes 1 mm in diameter which were able to be opened in aluminum with the drill because of fluid contact. Two of these drill holes act as an entrance to a flow cell, and they are formed in the center of the end face of the chamber inside. If a sensor platform is pressed to an O ring, two gratings of a sensor platform are located in the vestibule to these flow cells. The 3rd drill hole acts as an exit of a flow cell, and it is arranged so that an incidence grating may be symmetrically located between one side of the entrance of a flow cell, and an exit. Buffer solution is poured in into a cell through the entrance by the side of an incidence grating, and the quality of an analysis target subject is poured in into a flow cell through the entrance by the side of an outgoing radiation grating. By this composition, contamination of the incidence grating by the solution ingredient of the quality of an analysis target subject is prevented

(principle of a counterflow).
The sealed joint of a waveguide and a flow cell is realized by the O ring inserted in the flow cell. The medium in a flow cell can be replaced using the principle of a counterflow by hose connection.
A diode laser is used in order to form a convergent light beam. The laser beam with a diameter of 0.4 mm emitted from this laser optics device is always making the right angle with the end face of the sensor platform. It is possible to adjust the intensity of this laser beam and polarization using light polarizer and lambda/2 plate. A band-pass filter with a wavelength of 670 nm removes the photon which is emitted by the diode laser in the wavelength range (690-740 nm) of the fluorescent substance which should be detected, and bars fluorescence detection. The angle which this laser beam and the major axis of a waveguide make can be freely adjusted using a rotating element, and, thereby, the degree of incidence angle in the TE0 mode is adjusted. The focus is united with the center of the side of having met the major axis of the waveguide, on the level in the TE0 mode, and the optical apparatus for detection (C) forms the image in the mode on the surface of a waveguide on a detector. By the strip screen in front of a detector, only the field (namely, field (0.6 mm x 15 mm)) corresponding to the outside of the molecule fixed by the strip is projected. The optical apparatus for detection chosen seems to form the image of 1:1 on the surface of a waveguide in the field of a detector. Excitation light is removed substantially, and only a fluorescence photon is turned to a detector as a matter of fact, and it is made to pass with the combination of a filter (725 nm of 2x band passes).
B2.3 Implementation of multiple assay A flow cell is first filled with PBS7.0 and the degree of incidence angle is adjusted using a rotary unit. :1 washing buffer solution PBS7.0 which pours in the following solutions continuously through a flow cell for every measurement cycle One ml, Homo sapiens antibody by which the sign was carried out by Cy5.5 of nature of 2 analysis target subjects-10pM by flow 500microl./ 1 ml, It is [3 washing buffer solution PBS7.0 1ml and] 4 KAOTORO pick buffer solution (Grishin) by flow 250microl./by flow 250microl./. It is [pH2.6 1ml and] 5 washing buffer solution PBS7.0 by flow 250microl./. One ml, It is a counterflow by flow 500microl./:P BS7.0 A part for 5 ml and flow 300microl./ The multiple valve and piston pump by which computer control was carried out are used,

and conduction of the above-mentioned various solutions is carried out into a flow cell with an above-mentioned order and flow between the measurement cycles for 15 minutes.

The vertical position of a flow cell is adjusted with an advancing-side-by-side unit, and it is made first for the mode to be correctly settled in the upstream field on the surface of a waveguide. The Homo sapiens antibody by which the sign was carried out by Cy5.5 is beforehand fixed by this field. Since this strip is tinged with eternal fluorescence as a result of excitation by a laser beam, a vertical position is adjusted as a photon counter shows the maximum. Thereby, the position of the fixed Homo sapiens antibody by which Cy5.5 sign was carried out is identified.

Then, automatical measurement is started. In this measurement, by increment change of the vertical position of the flow cell by an advancing-side-by-side unit corresponding to the interval of the fixed strip, five strips are moved upwards with every one cycles of 8 seconds according to the above-mentioned order 1-5, and it doubles with the focus of a detector. The TE0 mode is formed only in said selected field of the above-mentioned shape.

While the flow cell is held with the waveguide at one place, the value measured for 1 second by the photon counter in said selected field is recorded as a function of time.

This automatic reciprocating movement between five different fields of a waveguide is continued over the measurement period for 15 minutes on the whole. The above-mentioned solution carries out conduction of the measuring cell with a proper flow during this period. The obtained data can be displayed as a function of time. The field (a strip / channel 1) where the Homo sapiens antibody by which Cy5.5 sign was carried out is fixed shows a fluorescence over the whole measurement cycle, and does not show 10pM solution and the interaction of the Homo sapiens antibody which were poured in into the measuring cell as quality of an analysis target subject and by which Cy5.5 sign was carried out. When protein A is the fields 2, 4, and 5 of the sensor platform fixed beforehand, increase up to 4 thru/or 5 times of the starting value of a fluorescence signal is started in 150 seconds.

The start of this increase relates to the time of the quality of an analysis

target subject being poured in into a flow cell, and mutual. Even if the signal in these channels carries out conduction of 1 ml of the washing buffer solution to a flow cell by a part for flow 250microl./in 400 seconds, it does not change as a matter of fact with a high value. This action is in agreement with a specific binding with the antibody by which the sign was carried out to protein A. BSA is beforehand fixed as a reference by the field 3 of the sensor platform. Since the Homo sapiens antibody which is used as quality of an analysis target subject and by which Cy5.5 sign was carried out does not react to BSA nonspecific, this strip/channel show a very low value during measurement, so that it may be expected.

DRAWINGS

[Drawing 1]

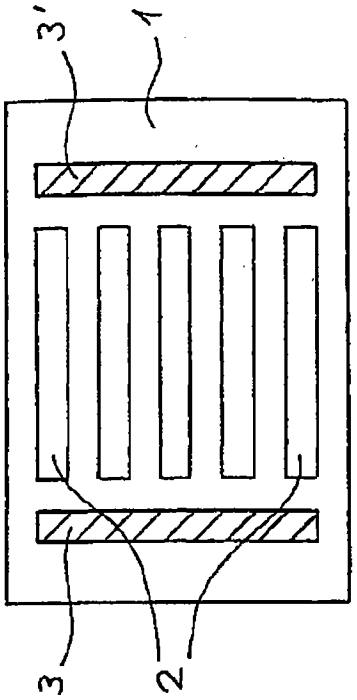

Fig. 1 b)

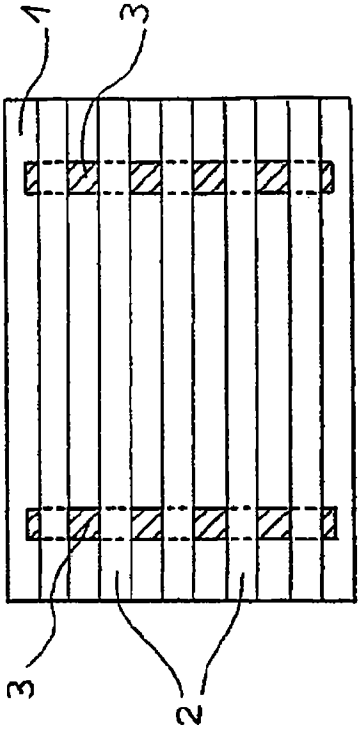

Fig. 1 d)

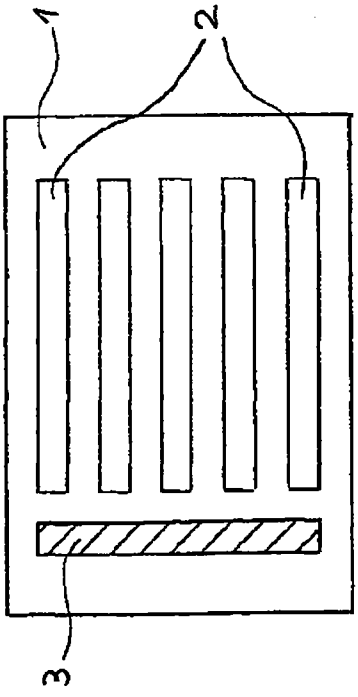

Fig. 1 a)

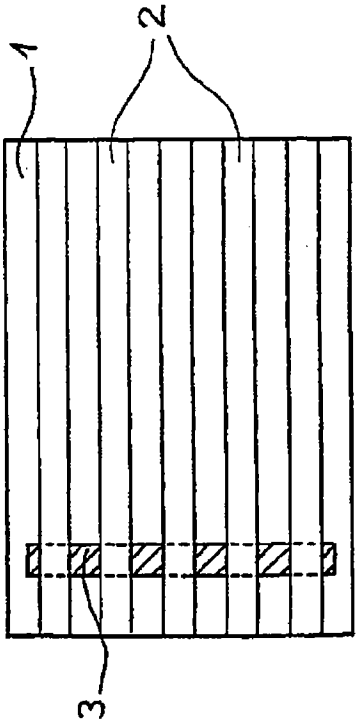

Fig. 1 c)

[Drawing 2]

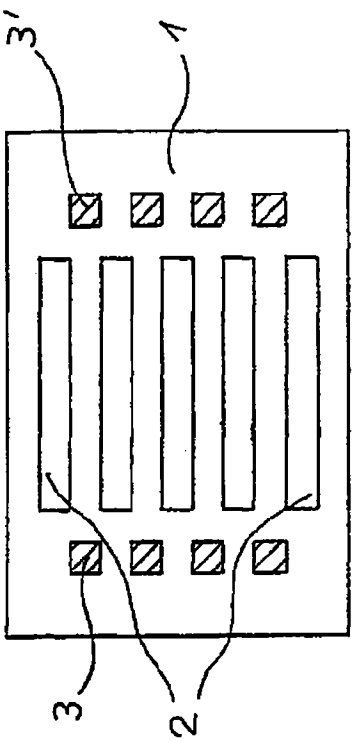

Fig. 2 b)

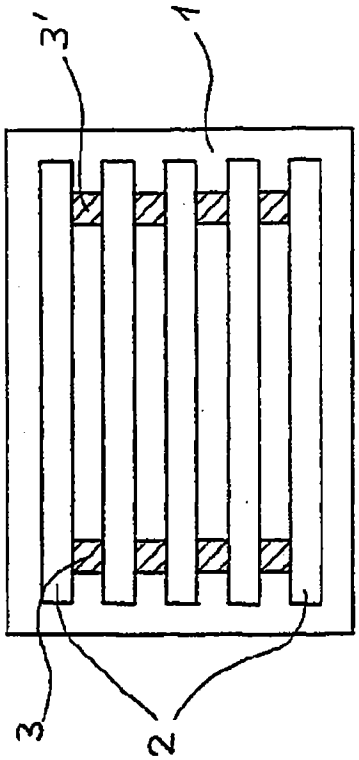

Fig. 2 d)

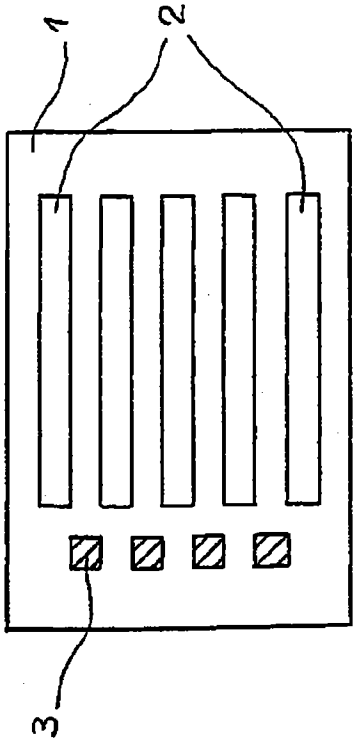

Fig. 2 a)

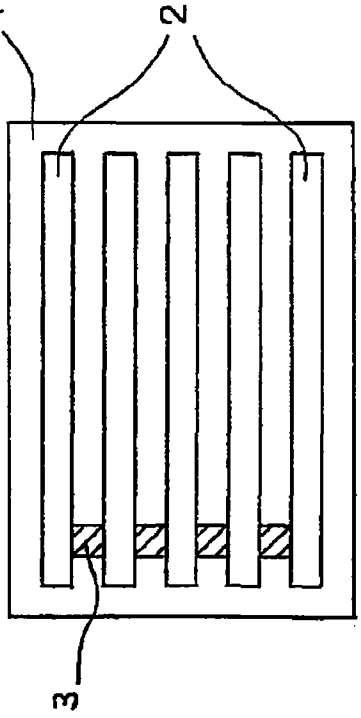

Fig. 2 c)

[Drawing 3]

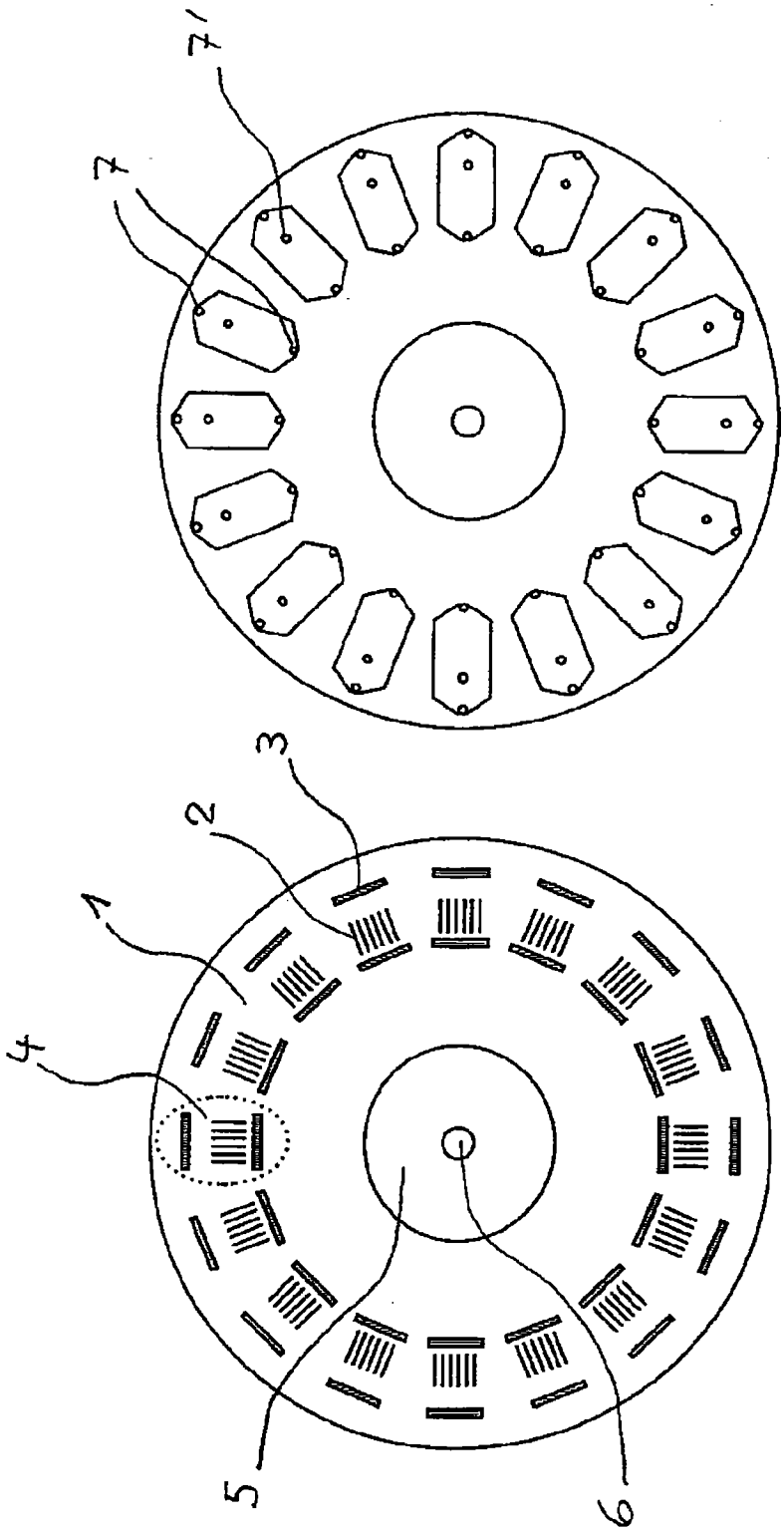

Fig. 3 b)

Fig. 3 a)

[Drawing 4]

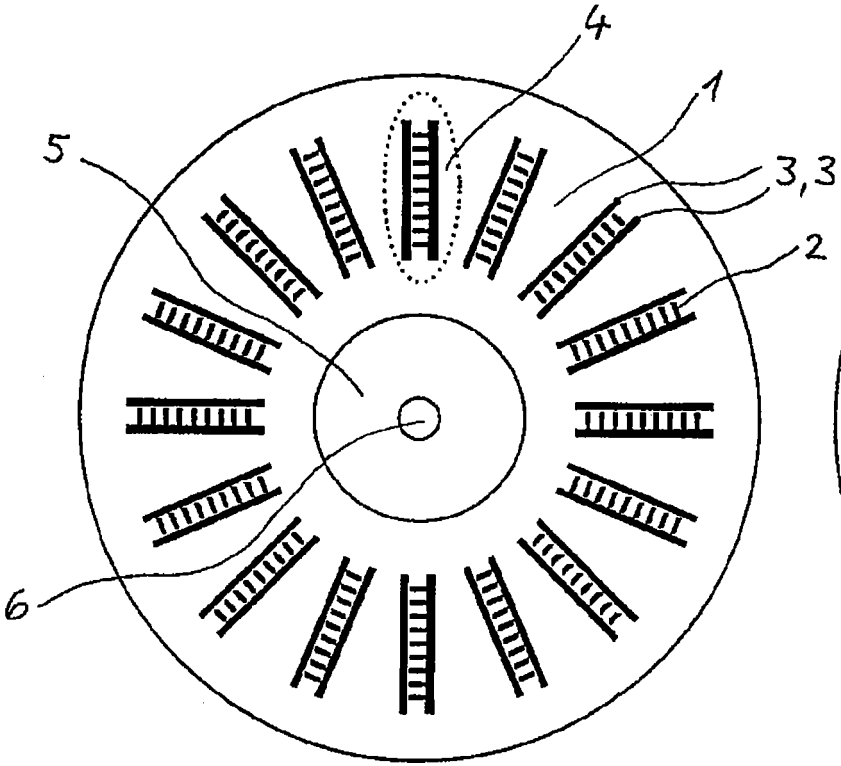

Fig. 4 a)

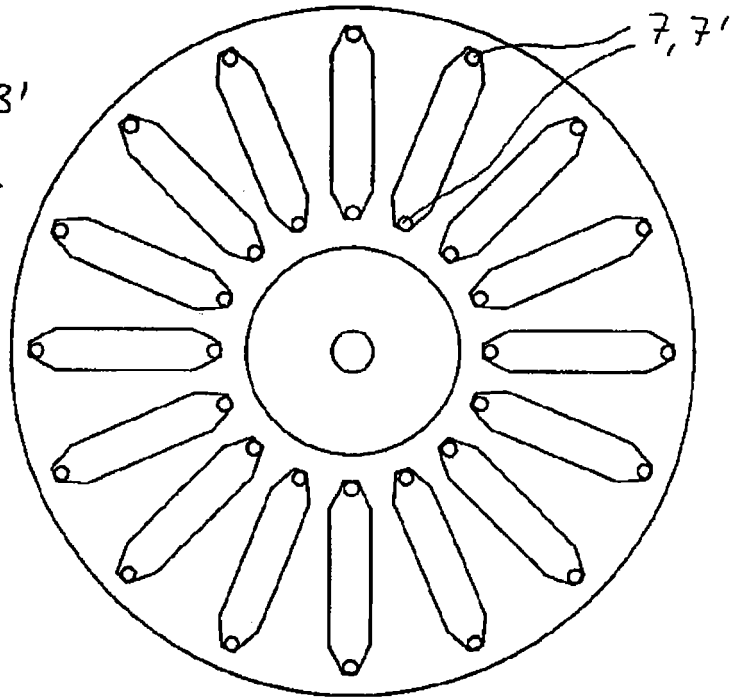

Fig. 4 b)

[Drawing 5]

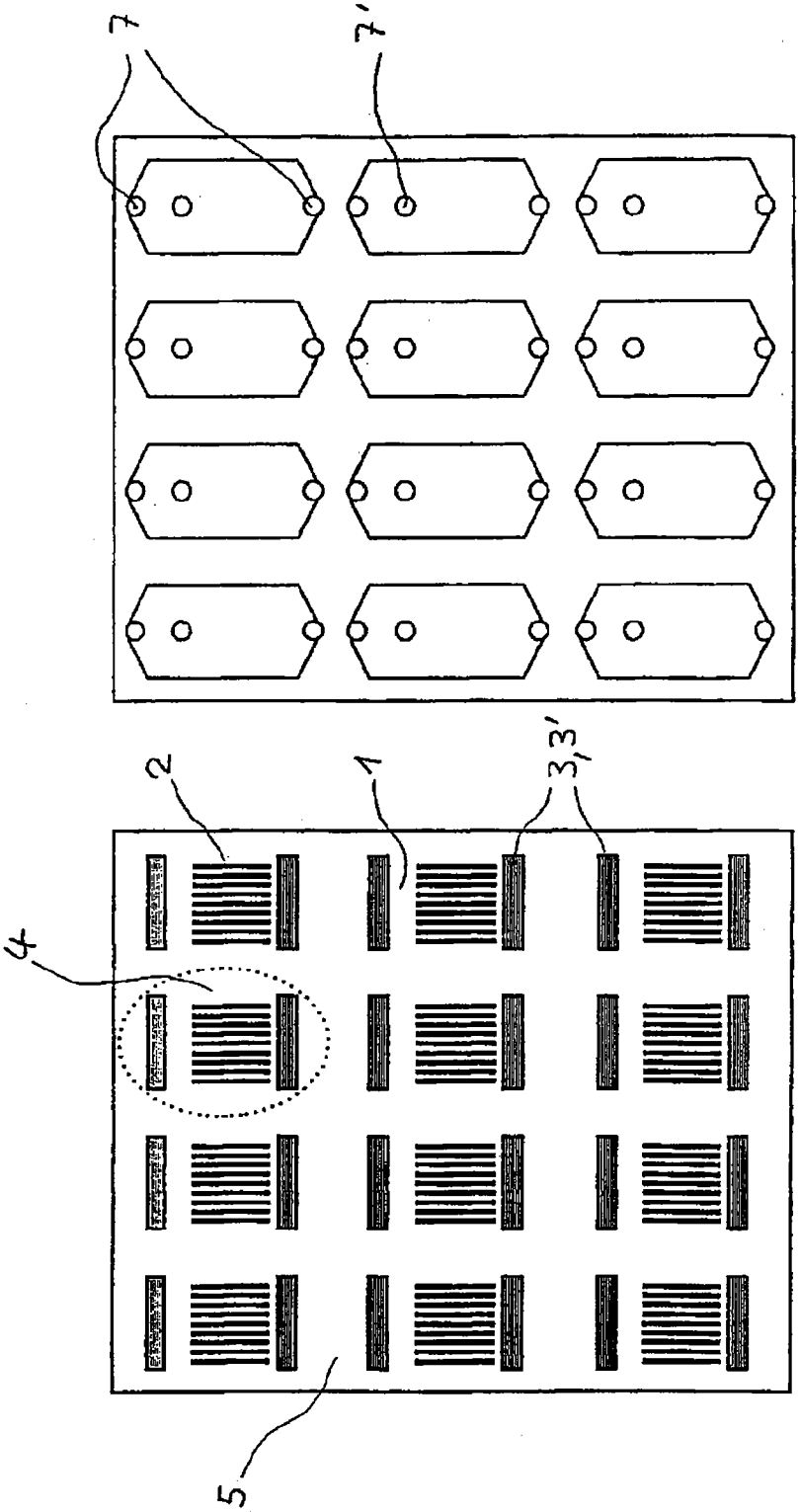

Fig. 5 b)

Fig. 5 a)

[Drawing 6]

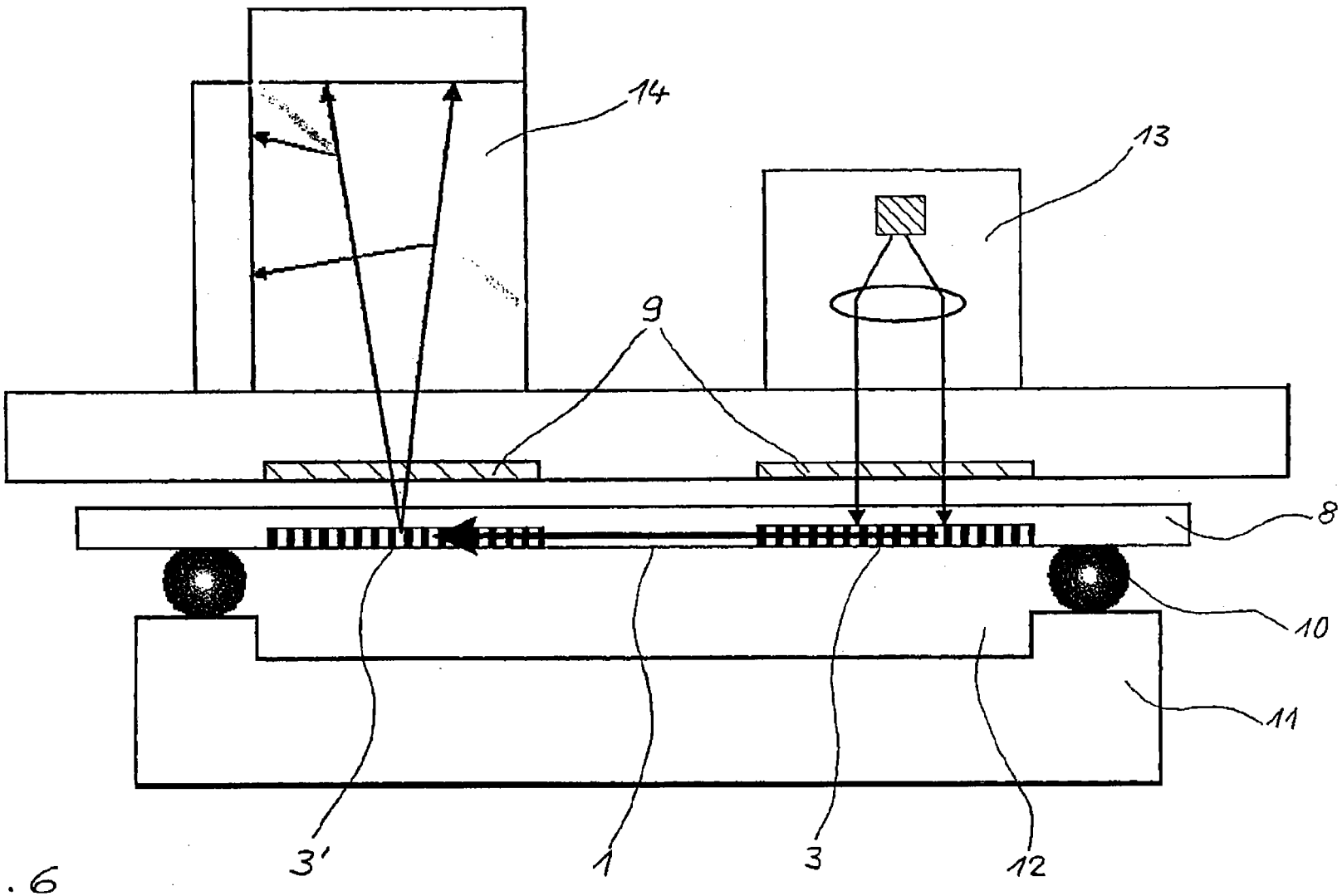

Fig. 6